

Supporting Information

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Structure–Activity Relationship Study Reveals ML240 and ML241 as Potent and Selective Inhibitors of p97 ATPase

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Raymond J. Deshaies^{*,[a]}

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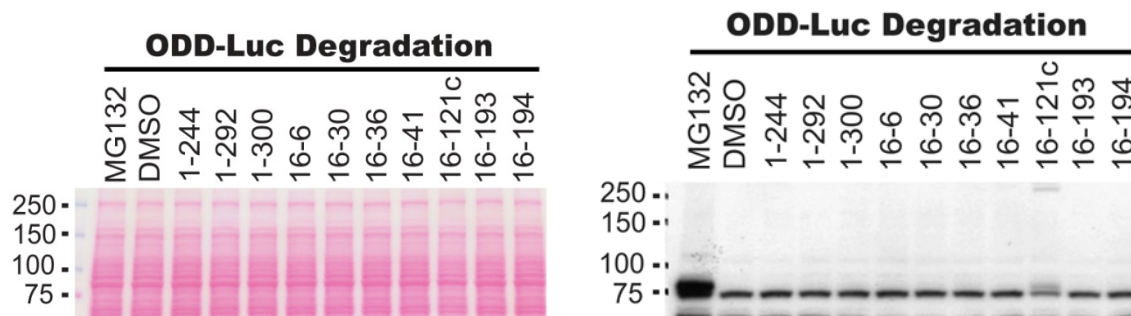
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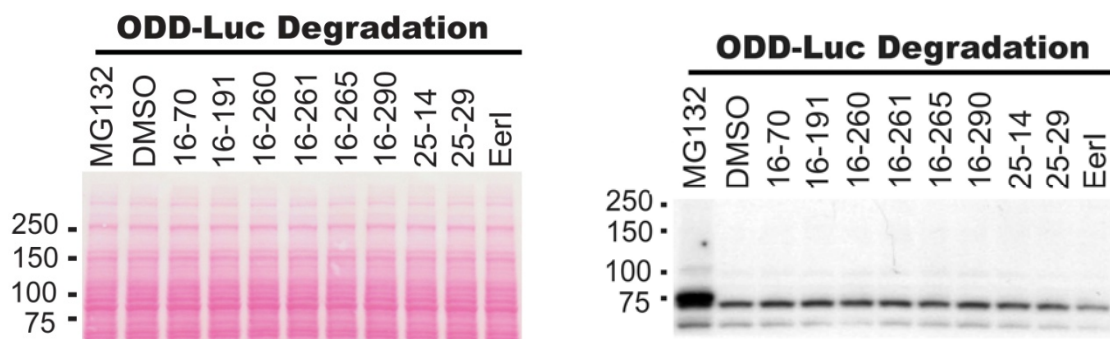
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A



B



C

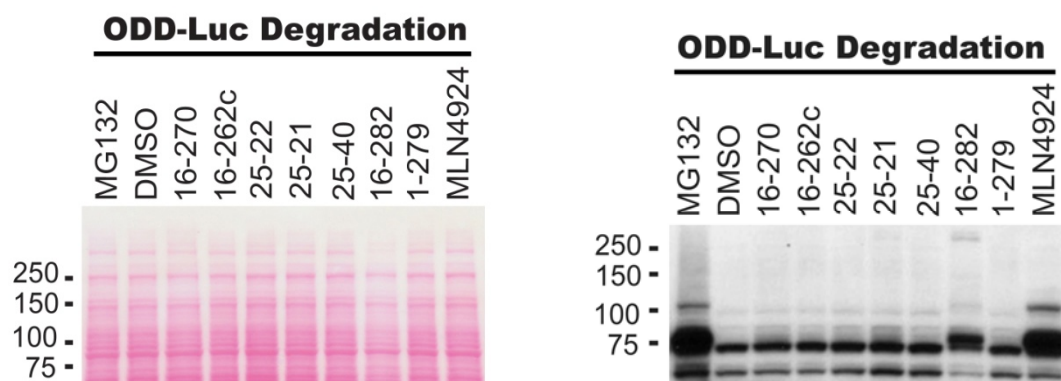


Figure S1. ODD-Luc degradation western blot assay. HeLa cells stably expressing the Ub^{G76V}-GFP and ODD-Luc reporters were grown in 6 well plates. Cells were treated with MG132 (4 μ M for 1 h) to accumulate reporter, washed, and exposed to the indicated test compounds plus CHX to initiate a chase. After 2h, cells were harvested and evaluated by immunoblotting for the remaining ODD-Luc (right panel). The Ponceau S-stained filters serve as loading controls (left panel). In the figure test compounds are identified using the “KU-SCC #”, where each two part identifier is prefixed with the letter code KSC. Compound structures can be found in the supplementary SAR Tables S1 to S11.

K4C107871N

p97 probes

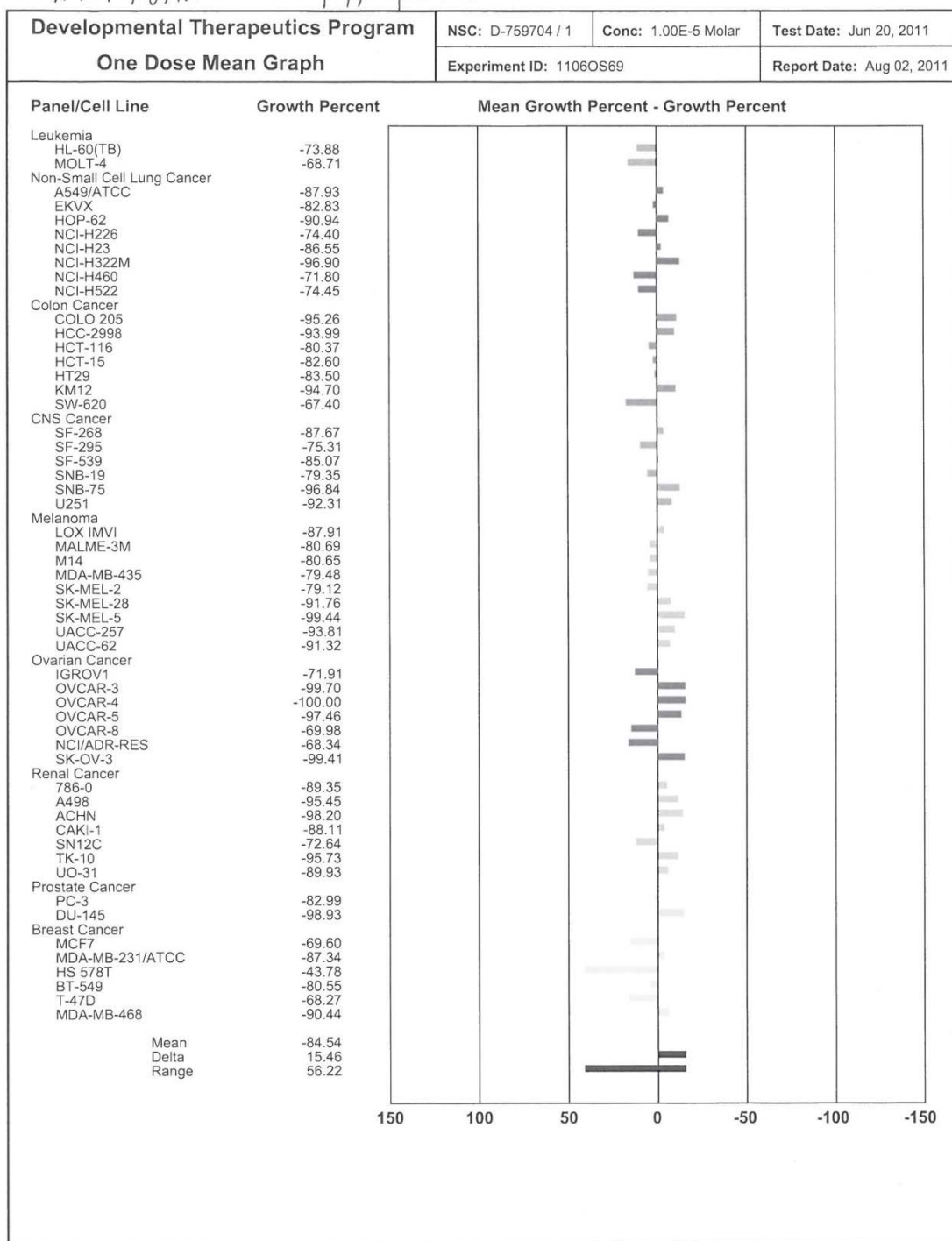


Figure S2: Full results from the NCI 60 cell line panel for **ML240**.

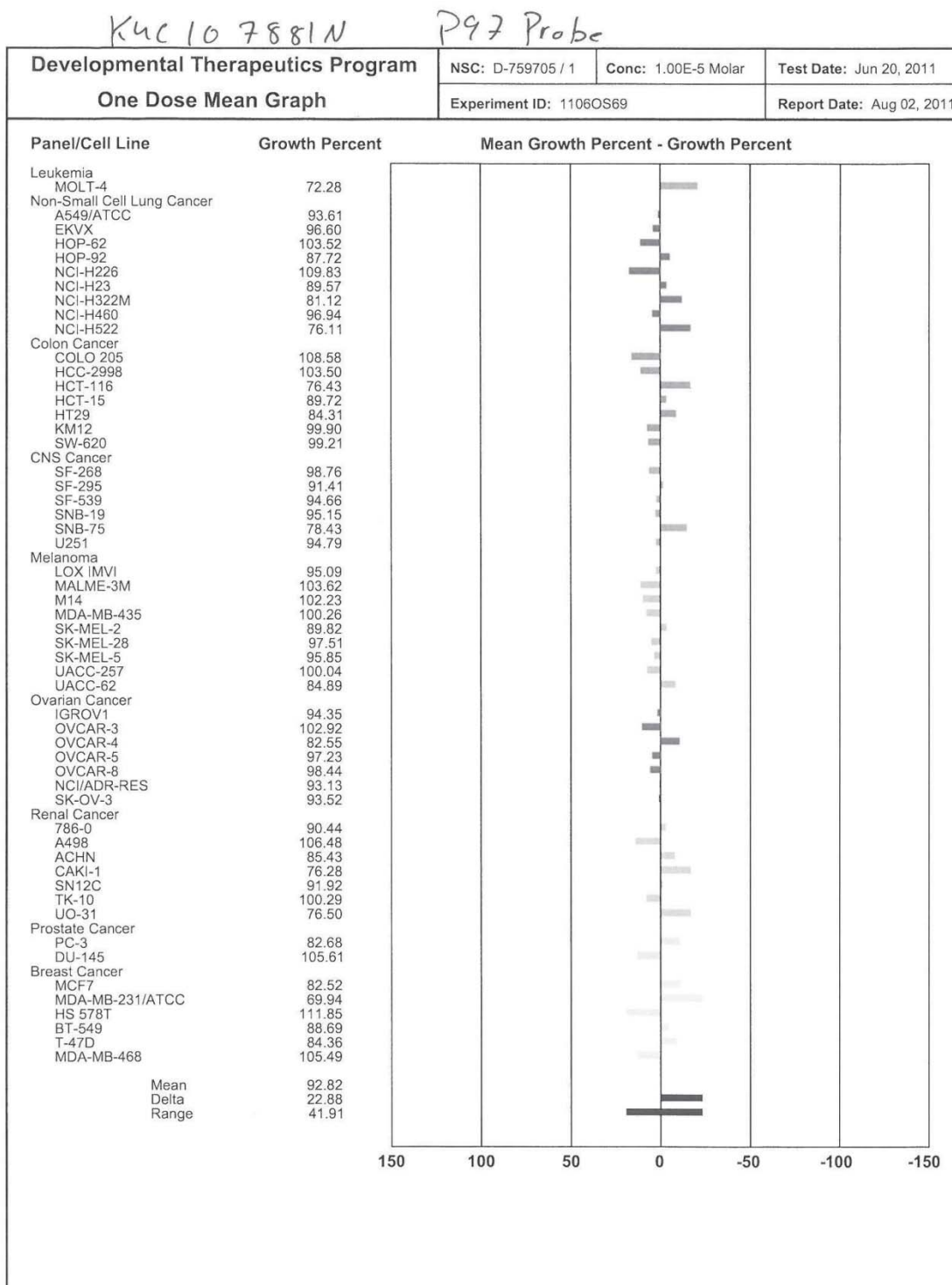
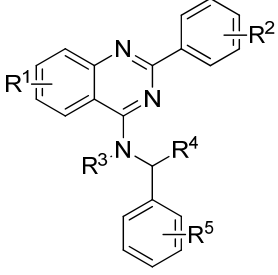


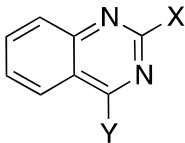
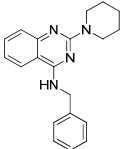
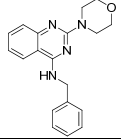
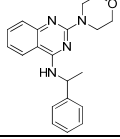
Figure S3: Full results from the NCI 60 cell line panel for **ML241**.

Table S1: Commercial analogues of *N*-benzyl-2-(2-fluorophenyl)quinazolin-4-amine

| compound identifiers | | | | |  | | | | | p97 inhibition | |
|-----------------------|----------|----------|---------------|---|--|-------------------|----|----|-------|---------------------------------|--|
| Cpd | CID | SID | KU SCC # | * | R1 | R2 | R3 | R4 | R5 | ATPase IC ₅₀ (μM) | Ub ^{G76V} -GFP IC ₅₀ (μM) |
| S1 1 [#] | 886813 | 87796231 | KSC-1- 150 | P | H | 2-F | H | H | H | 3±0.8 | 9.0±1.3 |
| S2 2 [#] | 1894007 | 87796228 | KSC-1- 146 | P | H | 2-Cl | H | H | H | 1.2±0.6 | 8±3 |
| S3 3 [#] | 2927831 | 87796230 | KSC-1- 149 | P | H | 3-NO ₂ | H | H | H | 5.9±3 | 4.0±1.6 |
| S4 | 780643 | 87796227 | KSC-1- 145 | P | H | H | H | H | H | 4.2±2.3 | 12±3 |
| S5 | 4084712 | 87796265 | KSC-1- 226 | P | H | 3-Me | H | H | H | 4.2±0.2 | 17±4 |
| S6 | 1591117 | 87796273 | KSC-1- 236 | P | H | 4-Cl | H | H | H | 5.5±1.9 | 20±3 |
| S7 | 1187251 | 87796271 | KSC-1- 234 | P | H | 4-NO ₂ | H | H | H | 11±6 | 19±7 |
| S8 | 949742 | 87796266 | KSC-1- 227 | P | H | 4-OMe | H | H | H | 1.6±0.3 | 15±2 |
| S9 | 3395671 | 87796263 | KSC-1- 224 | P | H | 4-Me | H | H | H | 5.7±0.7 | 13±2 |
| S10 | 2452802 | 87796251 | KSC-1- 212 | P | H | H | H | H | 4-F | 11±3 | 19±3 |
| S11 | 20963125 | 87796258 | KSC-1- 219 | P | H | 4-OMe | H | H | 4-F | 7.8±0.4 | 9.8±3 |
| S12 | 20963158 | 87796259 | KSC-1- 220 | P | H | 4-OMe | H | H | 4-OMe | 13±4 | 15±5 |
| S13 | 20963177 | 87796260 | KSC-1- 221 | P | H | 4-OMe | H | H | 4-Me | 8±2 | 12±2 |
| S14 | 20963187 | 87796261 | KSC-1- 222 | P | H | 4-OMe | H | H | 4-Cl | 8±2 | 9.3±1 |
| S15 | 20963255 | 87796262 | KSC-1- 223 | P | H | 4-Cl | H | H | 4-F | 8±0.2 | 20±5 |
| S16 | 4084711 | 87796264 | KSC-1- 225 | P | H | 3-Me | H | H | 4-F | 15±2 | 12±0.8 |
| S17 | 2790952 | 87796274 | KSC-1- 237 | P | H | 4-Me | H | Me | H | 7±4 | 17±4 |
| S18 | 15992808 | 87796255 | KSC-1- 216 | P | H | 2-F | H | Me | H | >30 | 15±4 |
| S19 4 [#] | 8074678 | 87796236 | KSC-1- 193 | P | 7-Cl | H | H | H | H | 70±24 | 12±4 |
| S20 5 [#] | 8080035 | 87796237 | KSC-1- 194 | P | 7-Cl | 4-Me | H | H | H | 39±13 | 24±5 |
| S21 | 8080040 | 87796238 | KSC-1- 195 | P | 7-Cl | 4-OMe | H | H | H | 25±11 | 70±30 |

| | | | | | | | | | | | |
|--|----------|----------|-----------|---|---|-------------------|-----------------|----|-------------------|---------|---------|
| S22 | 2454628 | 87796252 | KSC-1-213 | P | H | H | CH ₂ | H | 2-CH ₂ | >30 | 19±5 |
| S23 | 2047240 | 87796235 | KSC-1-147 | P | H | 4-Br | H | H | H | 72±14 | 25±10 |
| S24 | 2178012 | 87796229 | KSC-1-148 | P | H | 2-NO ₂ | Me | H | H | 25±11 | 11±6 |
| S25 | 1819025 | 87796240 | KSC-1-200 | P | H | 3,4-Di-Cl | H | H | H | 7.1±0.4 | 37±6 |
| S26 | 2452792 | 87796250 | KSC-1-211 | P | H | H | H | H | 3-Cl | 28±9 | 17±4 |
| S27 | 2465033 | 87796253 | KSC-1-214 | P | H | H | H | H | 2-Cl | 30±10 | 11±3 |
| S28 | 2456309 | 87796254 | KSC-1-215 | P | H | H | H | H | 4-Cl | >30 | 15±3 |
| S29 | 15993188 | 87796256 | KSC-1-217 | P | H | 2-F | H | H | 2-Cl | 26±12 | 15±3 |
| S30 | 15995431 | 87796257 | KSC-1-218 | P | H | 2-F | Me | H | H | 25±4 | 6.0±2.0 |
| S31 | 1566144 | 87796272 | KSC-1-235 | P | H | 4-NO ₂ | Me | H | H | 8.4±4 | 28±4 |
| S32 | 5051334 | 87796275 | KSC-1-238 | P | H | H | H | Me | H | 27±14 | 13±1 |
| S33 | 1895905 | 87796288 | KSC-1-257 | P | H | 2,4-Di-Cl | H | H | H | >30 | 11±0.8 |
| S34 8 [#] | 1553819 | 87796289 | KSC-1-258 | P | H | H | Me | H | H | 49±17 | 17±5 |
| * Designates whether a compound was purchased (P) or synthesized (S) # Compound identifier used in the main text. | | | | | | | | | | | |

Table S2: Analogues of *N*², *N*⁴-disubstitued quinazoline-2,4-diamine

| compound identifiers | | | | |  | p97 inhibition | |
|-----------------------|---------|----------|-----------|---|--|---------------------------------|--|
| Cpd | CID | SID | KU SCC # | * | structure | ATPase IC ₅₀ (μM) | Ub ^{G76V} -GFP IC ₅₀ (μM) |
| S35 6 [#] | 696840 | 87796233 | KSC-1-152 | P |  | 26±4 | 7.3±2 |
| S36 7 [#] | 832282 | 87796232 | KSC-1-151 | P |  | 23±6 | 36±9 |
| S37 | 2950240 | 87796276 | KSC-1-240 | P |  | 34±10 | 36±0.3 |

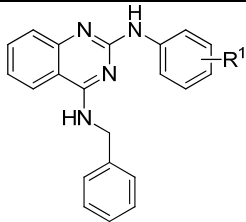
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|-----|----------|---------------|------------|---|--|-------|---------|
| S38 | 832283 | 92093143 | KSC-1-260 | P | | 53±18 | 31±6 |
| S39 | 1330669 | 87796248 | KSC-1-208 | P | | 34±11 | 35±5 |
| S40 | 1337599 | 92093137 | KSC-1-203 | P | | 33±8 | 12±1 |
| S41 | 1091839 | 92093140 | KSC-1-242 | P | | 57±15 | 56±10 |
| S42 | 2955641 | 87796277 | KSC-1-241 | P | | 22±12 | 39±18 |
| S43 | 5051334 | 87796275 | KSC-1-239 | P | | 43±13 | 70±16 |
| S44 | 2932797 | 92093142 | KSC-1-254 | P | | 30±6 | 34±6 |
| S45 | 46873814 | 99313590 | KSC-16-190 | S | | >30 | 8.1±1.8 |
| S46 | 49830268 | 10390417 0 | KSC-16-272 | S | | >30 | >20 |

| | | | | | | | |
|--|----------|---------------|------------|---|--|------|-------|
| S47 | 49830259 | 10390417 3 | KSC-16-277 | S | | 7±3 | >20 |
| S48 | 49852179 | 10422194 4 | KSC-25-10 | S | | 31±7 | 47±9 |
| S49 | 49852178 | 10422194 6 | KSC-25-16 | S | | >30 | 45±18 |
| * Designates whether a compound was purchased (P) or synthesized (S) # Compound identifier used in the main text. | | | | | | | |

Table S3: Analogues of N^2 , N^4 -diphenylquinazoline-2,4-diamine

| compound identifiers | | | | | | | p97 inhibition | |
|--|----------|----------|------------|---|-------|-------|---------------------------------|--|
| Cpd | CID | SID | KU SCC # | * | R1 | R2 | ATPase IC ₅₀ (μM) | Ub ^{G76V} -GFP IC ₅₀ (μM) |
| S50 | 17324423 | 99239924 | KSC-16-149 | S | 4-OMe | 4-OMe | 22±4 | 23±3 |
| S51 | 46850879 | 99239936 | KSC-16-163 | S | 3-Cl | H | 34±16 | 12±2 |
| S52 | 46850870 | 99239937 | KSC-16-164 | S | 3-Cl | 4-OMe | 34±14 | 13±1 |
| S53 | 46850872 | 99239940 | KSC-16-174 | S | 3-Cl | 4-Me | 49±19 | 30±4 |
| S54 | 46850878 | 99239942 | KSC-16-176 | S | 3-Cl | 4-Cl | 117±5.8 | 21±2 |
| S55 | 46850875 | 99239944 | KSC-16-151 | S | 4-Me | 4-Me | 54±19 | 21±4 |
| S56 9 [#] | 213847 | 99206554 | KSC-16-146 | S | H | H | 2.6±0.8 | 7.2±1 |
| S57 | 1878549 | 87796278 | KSC-1-243 | P | 4-Cl | 4-Cl | 52±10 | 19±4 |
| * Designates whether a compound was purchased (P) or synthesized (S) # Compound identifier used in the main text. | | | | | | | | |

Table S4 : Analogues of *N*⁴-benzyl-*N*²-phenylquinazoline-2,4-diamine

| compound identifiers | | | | |  | p97 inhibition | |
|------------------------|----------|----------|------------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R1 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S58 10 [#] | 2909934 | 87796234 | KSC-1-153 | P | H | 2.3±1 | 3.1±0.4 |
| S59 | 929548 | 87796285 | KSC-1-251 | P | 4-Me | 2.2±0.4 | 6.3±1.4 |
| S60 | 2351737 | 87796281 | KSC-1-246 | P | 4-Cl | 5.4±2 | 5.9±1.2 |
| S61 | 797650 | 87796284 | KSC-1-249 | P | 4-F | 3.8±1.2 | 9.4±1 |
| S62 | 1943389 | 87796280 | KSC-1-245 | P | 4-Br | 1.8±0.4 | 6.0±0.8 |
| S63 | 1330474 | 92093141 | KSC-1-250 | P | 4-OMe | 3.8±0.5 | 4.5±1.1 |
| S64 | 949445 | 87796286 | KSC-1-252 | P | 2-Me | 3.4±1.5 | 10±2 |
| S65 | 886196 | 87796282 | KSC-1-247 | P | 2-F | 0.85±0.17 | 10±2 |
| S66 | 1415819 | 87796283 | KSC-1-248 | P | 2-OMe | 2.2±0.9 | 11±3 |
| S67 | 950033 | 87796287 | KSC-1-253 | P | 3-Me | 1.7±0.5 | 3.0±0.7 |
| S68 11 [#] | 1633082 | 87796279 | KSC-1-244 | P | 3-Cl | 0.48±0.16 | 7.8±1.3 |
| S69 | 1571079 | 87796290 | KSC-1-259 | P | 3,4-di-Cl | 8.1±2.6 | 12±2 |
| S70 | 1330474 | 92252642 | KSC-1-290 | S | 4-OMe | 3.5±0.5 | 4.8±0.7 |
| S71 | 45108365 | 92252645 | KSC-1-293 | S | 3-Br | 2.5±0.5 | 4.3±0.8 |
| S72 | 39861404 | 92252643 | KSC-1-291 | S | 3-OMe | 2.5±0.2 | 4.3±0.7 |
| S73 | 46850871 | 99239933 | KSC-16-155 | S | 3-NO ₂ | 5.2±0.5 | 19±2 |
| S74 44 [#] | 11645888 | 92252644 | KSC-1-292 | S | 3-F | 1.6±0.1 | 2.7±0.4 |
| S75 | 45108364 | 92252647 | KSC-1-295 | S | 3-Cl-6-F | 13±3 | 13±2 |
| S76 | 45108364 | 92252647 | KSC-1-294 | S | 3,5-di-Cl | 8.2±0.3 | 13±1 |
| S77 | 46224527 | 96079523 | KSC-16-103 | S | 3-Cl-2-OMe | 0.9±0.2 | 6.3±1.7 |
| S78 | 46224522 | 96079524 | KSC-16-104 | S | 3-F-2-Me | 0.9±0.1 | 3.7±0.8 |
| S79 | 46224524 | 96079525 | KSC-16-105 | S | 3-F-5-Me | 0.7±0.05 | 5.4±0.8 |

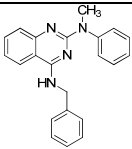
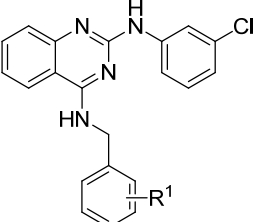
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|--|----------|----------|------------|---|---|----------|---------|
| S80 | 46224529 | 96079526 | KSC-16-106 | S | 3-F-2-OMe | 1.7±0.5 | 12±3 |
| S81 | 46224523 | 96079527 | KSC-16-107 | S | 3-Cl-2-Me | 0.7±0.1 | 5.5±1 |
| S82 | 46224519 | 96079528 | KSC-16-108 | S | 3-F-6-Me | 0.8±0.1 | 5±1 |
| S83 | 46224528 | 96079529 | KSC-16-109 | S | 3-F-4-Me | 0.9±0.2 | 5.2±1.2 |
| S84 | 46224530 | 96079530 | KSC-16-110 | S | 3-F-4-OMe | 0.9±0.1 | 4.7±0.8 |
| S85 | 46224526 | 96079531 | KSC-16-112 | S | 3-Cl-6-Me | 0.8±0.07 | 7±1.5 |
| S86 | 46224518 | 96079532 | KSC-16-113 | S | 3-Cl-6-OMe | 1.1±0.2 | 16±6 |
| S87 | 46829342 | 99206553 | KSC-16-120 | S | 3-F-6-OMe | 6.7±3 | 9.3±1 |
| S88 | 45108363 | 92252640 | KSC-1-288 | S | 2-Br | 64±24 | 13±2 |
| S89 | 2384230 | 92252641 | KSC-1-289 | S | 2-Cl | 69±25 | 13±2 |
| S90 | 46829335 | 99239925 | KSC-16-150 | S | 3-CF ₃ | 50±16 | 21±1 |
| S91 | 46850881 | 99239930 | KSC-16-152 | S | 3-I | 5.2±1.9 | 36±4 |
| S92 | 46873821 | 99313588 | KSC-16-188 | S |  | >30 | 9.2±1.2 |
| * Designates whether a compound was purchased (P) or synthesized (S) # Compound identifier used in the main text. | | | | | | | |

Table S5: Analogues of *N*⁴-benzyl-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine

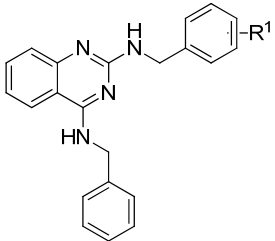
| compound identifiers | | | | |  | p97 inhibition | |
|------------------------|----------|----------|------------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R1 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S93 | 46173070 | 96022083 | KSC-16-72 | S | 4-Me | 1.4±0.3 | 12±2 |
| S94 | 46173066 | 96022090 | KSC-16-89 | S | 4-Cl | 2.8±0.9 | 7.6±2.4 |
| S95 12 [#] | 46173057 | 96022093 | KSC-16-98 | S | 4-F | 1.5±0.3 | 5.7±1.3 |
| S96 | 46173059 | 96022096 | KSC-16-101 | S | 4-Br | 7.4±2 | 10±3 |
| S97 | 46173063 | 96022086 | KSC-16-79 | S | 4-OMe | 2.3±0.6 | 11±4 |

| | | | | | | | |
|------|----------|----------|------------|---|-------|---------|---------|
| S98 | 46173069 | 96022080 | KSC-16-63 | S | 2-Me | 4.2±1.1 | 11±3 |
| S99 | 46173062 | 96022087 | KSC-16-84 | S | 2-Cl | 4.7±1.4 | 18±5 |
| S100 | 46173072 | 96022091 | KSC-16-92 | S | 2-F | 1.8±0.5 | 7.8±2.1 |
| S101 | 46173058 | 96022094 | KSC-16-99 | S | 2-Br | 4±1.7 | 12±5 |
| S102 | 46173067 | 96022084 | KSC-16-75 | S | 2-OMe | 1.6±0.4 | 11±2 |
| S103 | 46173061 | 96022081 | KSC-16-66 | S | 3-Me | 2.3±0.6 | 9.7±2.7 |
| S104 | 46173068 | 96022088 | KSC-16-87 | S | 3-Cl | 5±1.2 | 15±4 |
| S105 | 46173060 | 96022092 | KSC-16-95 | S | 3-F | 1.2±0.2 | 6.3±1.7 |
| S106 | 46173065 | 96022095 | KSC-16-100 | S | 3-Br | 3.7±0.9 | 9.9±2 |
| S107 | 46173071 | 96022085 | KSC-16-78 | S | 3-OMe | 1±0.1 | 9.9±1.6 |

* Designates whether a compound was purchased (P) or synthesized (S)

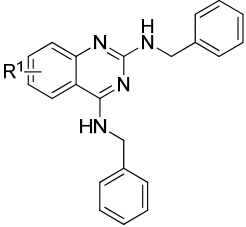
Compound identifier used in the main text.

Table S6: Analogues of N^2,N^4 -dibenzylquinazoline-2,4-diamine (DBeQ)

| compound identifiers | | | | |  | p97 inhibition | |
|-------------------------|----------|----------|-----------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R1 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S108 13 [#] | 45382111 | 93374187 | KSC-16-2 | S | 4-OMe | 3±0.5 | 1.3±0.2 |
| S109 45 [#] | 25144450 | 93374186 | KSC-1-300 | S | 4-Me | 3±0.3 | 1.5±0.4 |
| S110 | 45382112 | 93374224 | KSC-16-33 | S | 4-Cl | 3.1±0.2 | 2.1±0.4 |
| S111 | 45382121 | 93374227 | KSC-16-38 | S | 4-F | 2.6±0.2 | 3.4±0.5 |
| S112 | 45382119 | 93374230 | KSC-16-42 | S | 4-Br | 4.3±0.9 | 3.9±0.3 |
| S113 | 45382120 | 93374191 | KSC-16-8 | S | 2-Me | 2.7±0.5 | 1.9±0.4 |
| S114 | 45382117 | 93374222 | KSC-16-31 | S | 2-Cl | 5.3±1.2 | 2.9±0.9 |

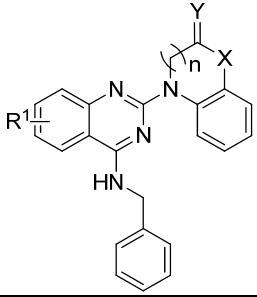
| | | | | | | | |
|--|----------|----------|-----------|---|------------------------|---------|---------|
| S115 | 45382108 | 93374225 | KSC-16-35 | S | 2-F | 2.9±0.4 | 2.8±0.4 |
| S116 | 45382107 | 93374228 | KSC-16-40 | S | 2-Br | 2.0±0.3 | 3.8±0.7 |
| S117 | 45382105 | 93374193 | KSC-16-29 | S | 2-OMe | 3.6±0.8 | 1.9±0.2 |
| S118 | 45382113 | 93374192 | KSC-16-28 | S | 3-Me | 2.3±0.4 | 2.5±0.5 |
| S119 | 45382114 | 93374223 | KSC-16-32 | S | 3-Cl | 2.7±0.1 | 2.5±0.4 |
| S120 46 [#] | 45382109 | 93374190 | KSC-16-6 | S | 4-CF ₃ | 2.6±0.4 | 2.3±0.3 |
| S121 47 [#] | 45382116 | 93374221 | KSC-16-30 | S | 3-OMe | 4.5±0.8 | 2.5±0.8 |
| S122 48 [#] | 45382110 | 93374226 | KSC-16-36 | S | 3-F | 3.1±0.4 | 2.8±0.4 |
| S123 49 [#] | 45382118 | 93374229 | KSC-16-41 | S | 3-Br | 3.7±0.4 | 2.8±0.4 |
| S124 | 45382106 | 93374188 | KSC-16-3 | S | 3,4-di-Cl | 3±0.5 | 1.9±0.2 |
| S125 | 45382115 | 93374189 | KSC-16-4 | S | 4-Cl-3-CF ₃ | 4.7±1 | 2.2±0.4 |
| * Designates whether a compound was purchased (P) or synthesized (S) | | | | | | | |
| [#] Compound identifier used in the main text. | | | | | | | |

Table S7: Analogues of *N*²,*N*⁴-dibenzylquinazoline-2,4-diamine (DBeQ)

| compound identifiers | | | | |  | p97 inhibition | |
|-------------------------|----------|----------|-------------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R1 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S126 | 46224525 | 96079533 | KSC-16-114 | S | 5-Cl | 2.2±0.7 | 16±2 |
| S127 | 46224521 | 96079534 | KSC-16-115 | S | 5-F | 1.2±0.3 | 13±2 |
| S128 | 46224520 | 96079535 | KSC-16-117 | S | 6-Cl | 1.6±0.4 | 6.6±0.9 |
| S129 | 5276745 | 96022097 | KSC-16-102 | S | 6,7-di-OMe | 4.4±1.8 | 8.8±1.5 |
| S130 14 [#] | 46829340 | 99206522 | KSC-16-121c | S | 8-OMe | 0.6±0.06 | 10±2 |
| S131 | 46829333 | 99206552 | KSC-16-118 | S | 7-Me | 2.2±0.4 | 6.1±1.6 |

| | | | | | | | |
|--|----------|----------|-------------|---|-------------------|---------|---------|
| S132 | 46850874 | 99239928 | KSC-16-160c | S | 7-CF ₃ | 9.1±2 | 19±1 |
| S133 | 46850882 | 99239931 | KSC-16-153 | S | 8-Br | 3.3±0.9 | 30±2 |
| S134 | 46850883 | 99239932 | KSC-16-154 | S | 8-F | 3.1±0.5 | 18±2 |
| S135 | 46850884 | 99239934 | KSC-16-156 | S | 7-F | 2.6±0.5 | 6.1±0.8 |
| S136 | 46850880 | 99239935 | KSC-16-159 | S | 7-Cl | 5.5±0.9 | 6.3±0.9 |
| S137 | 46850885 | 99239938 | KSC-16-166 | S | 7-OMe | 5.7±1 | 42±6 |
| S138 | 46850877 | 99239939 | KSC-16-172 | S | 6-OMe | 7.5±1.1 | 8.6±1.7 |
| S139 | 46850873 | 99239941 | KSC-16-175 | S | 6-F | 4.7±0.4 | 8.2±1.5 |
| S140 | 4685087 | 99239943 | KSC-16-122 | S | 7-Br | 22±4 | 10±2 |
| S141 | 46850869 | 99239929 | KSC-16-167C | S | 7-CN | 25±10 | 21±3 |
| * Designates whether a compound was purchased (P) or synthesized (S) | | | | | | | |
| # Compound identifier used in the main text. | | | | | | | |

Table S8: *N*² Constrained DBeQ analogues

| compound identifiers | | | | |  | | | | p97 inhibition | |
|-------------------------|----------|----------|------------|---|--|---|----|----|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R1 | n | X | Y | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S142 | 46829336 | 99239922 | KSC-16-125 | S | H | 1 | C | -H | 4.4±1.8 | 10±2 |
| S143 | 46829332 | 99239923 | KSC-16-144 | S | H | 0 | C | -H | 2±0.5 | 11±3 |
| S144 15 [#] | 46173064 | 96022082 | KSC-16-70 | S | H | 1 | O | -H | 0.6±0.2 | 7±1.9 |
| S145 | 46829338 | 99206557 | KSC-16-147 | S | H | 1 | NH | -H | 0.4±0.05 | 6.3±1 |
| S146 | 46873816 | 99313586 | KSC-16-182 | S | 8-OMe | 1 | NH | -H | 0.9±0.1 | 3.7±0.2 |
| S147 38 [#] | 46873819 | 99313591 | KSC-16-191 | S | 8-OMe | 1 | O | -H | 0.2±0.02 | 3.3±0.4 |

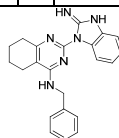
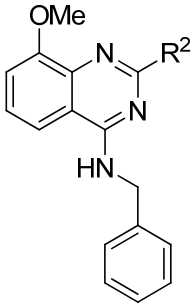
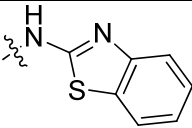
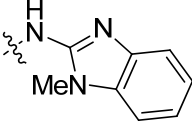
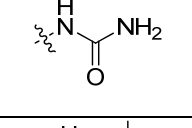
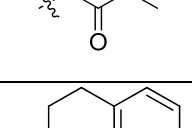
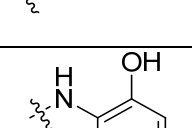
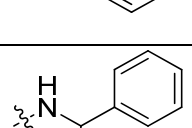
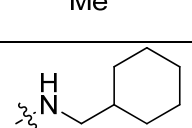

| | | | | | | | | | | |
|--|--------------|-----------|-----------------------|---|---|---|-------|-----|----------------|---------|
| S148 | 469312 12 | 99437738 | KSC-16-232 | S | 8-OH | 1 | O | -H | 1.2±0.3 | 7.7±1.7 |
| S149 | 498302 64 | 103904180 | KSC-16-255 | S | 8-Ph | 1 | O | -H | 3.5±0.6 | 5±0.9 |
| S150 33 [#] | 498302 53 | 103904181 | KSC-16-260 | S | 8- OCH ₂ CH ₂ OH | 1 | O | -H | 0.17±0.0 5 | 3.8±0.8 |
| S151 34 [#] | 498521 81 | 104221957 | KSC-25-29 | S | 8- OCH ₂ CH ₂ OMe | 1 | O | -H | 0.6±0.03 | 6.5±0.7 |
| S152 35 [#] | 498302 65 | 103904183 | KSC-16-265 | S | 8- OCH ₂ CH ₂ NEt ₂ | 1 | O | -H | 0.4±0.08 | 5.3±0.6 |
| S153 36 [#] | 498302 67 | 103904184 | KSC-16-268 | S | 8-p- OMePh | 1 | O | -H | 1.1±0.1 | 9±1 |
| S154 37 [#] | 498521 71 | 104221958 | KSC-25-30 | S | 8- <i>n</i> -Bu | 1 | O | -H | 2.63±0.7 | 28±3 |
| S155 39 [#] | 509185 89 | 113284765 | KSC-206- 005 | S | 8- OCH ₂ CN | 1 | O | -H | 0.4±0.08 | 7.7±0.7 |
| S156 | 498521 77 | 104221952 | KSC-25-17 | S | 8-OMe | 1 | NMe | -H | 3.1±0.5 | 7.8±0.7 |
| S157 | 498521 73 | 104221953 | KSC-25- 15c1 | S | 8-OMe | 1 | NCOMe | -H | 2.7±0.6 | 8±1 |
| S158 ML240 [#] | 498302 58 | 103904169 | KSC-16-270 (ML240) | S | 8-OMe | 0 | NH | =NH | 0.11±0.0 3 | 0.9±0.1 |
| S159 | 498302 70 | 103904172 | KSC-16- 262cc | S | 8-OMe | 0 | O | =O | 0.11±0.0 3 | 5±1 |
| S160 | 498521 76 | 104221943 | KSC-25-3 | S | 8-OMe | 0 | N** | -H | 3.3±1.1 | 78±45 |
| S161 18 [#] | 509185 80 | 113284753 | KSC-25-31 | S |  | | | | 0.05±0.0 03 | 1.8±0.2 |
| * Designates whether a compound was purchased (P) or synthesized (S) | | | | | | | | | | |
| ** unsubstituted nitrogen of a benzimidazole moiety | | | | | | | | | | |
| # Compound identifier used in the main text. | | | | | | | | | | |

Table S9: Alternatives to the quinazoline scaffold analogues

| compound identifiers | | | | | structure | p97 inhibition | |
|--|--------------|---------------|-----------------------|---|-------------------|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | Formulas X to XII | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| ML241[#] | 498302 60 | 103904 185 | KSC-16-290 (ML241) | S | | 0.11±0.0 3 | 3.5±0.4 |
| S162 17[#] | 498521 84 | 104221 950 | KSC-25-14 | S | | 0.4±0.1 | 6.4±1 |
| S163 31[#] | 498521 72 | 104221 955 | KSC-25-24 | S | | 1.1±0.2 | 10±1 |
| S164 | 509185 81 | 113284 766 | KSC-25-32 | S | | 2.8±0.6 | 14±3 |
| S165 32[#] | 498521 80 | 104221 956 | KSC-25-28 | S | | 2.9±0.2 | 27±3 |
| * Designates whether a compound was purchased (P) or synthesized (S) | | | | | | | |
| [#] Compound identifier used in the main text. | | | | | | | |

Table S10: Miscellaneous 8-methoxyquinazoline analogues

| compound identifiers | | | | |  | p97 inhibition | |
|-------------------------|----------|-----------|------------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R2 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S166 | 49852185 | 104221947 | KSC-25-22 | S |  | 0.5±0.2 | 14±2 |
| S167 19 [#] | 49852183 | 104221949 | KSC-25-21 | S |  | 0.3±0.07 | 7.8±1.2 |
| S168 | 49852174 | 104221945 | KSC-25-12 | S |  | 49±10 | 108±31 |
| S169 | 49852175 | 104221954 | KSC-25-19 | S |  | 60±23 | 37±7 |
| S170 20 [#] | 25144452 | 99313587 | KSC-16-187 | S |  | 15±3 | 7±1.3 |
| S171 | 46931213 | 99437735 | KSC-16-203 | S |  | 2.6±0.4 | 2.8±0.5 |
| S172 | 49830269 | 103904171 | KSC-16-273 | S |  | 12±5 | 2.1±0.7 |
| S173 | 49830255 | 103904174 | KSC-16-278 | S |  | 5.4±0.9 | 4.2±1 |

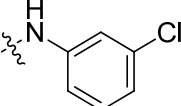
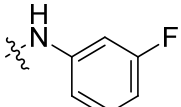
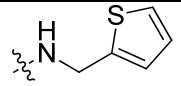
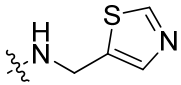
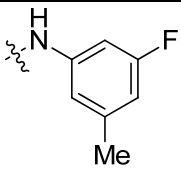
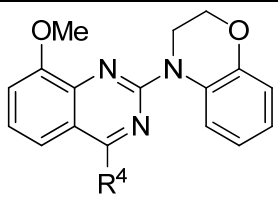
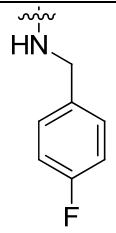
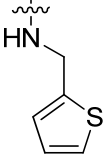
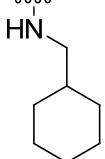
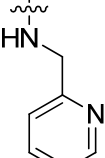
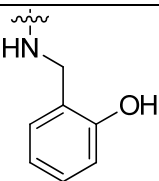
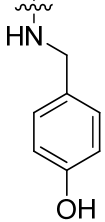
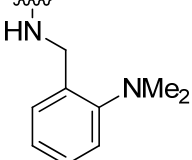
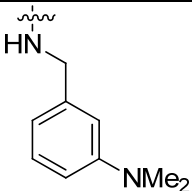
| | | | | | | | |
|--|----------|-----------|------------|---|--|-----------|---------|
| S174 50 [#] | 46873815 | 99313592 | KSC-16-193 | S |  | 0.5±0.1 | 5.4±1 |
| S175 51 [#] | 46873818 | 99313593 | KSC-16-194 | S |  | 0.52±0.04 | 4.8±0.7 |
| S176 52 [#] | 49830257 | 103904175 | KSC-16-282 | S |  | 1.7±0.4 | 1.8±0.3 |
| S177 | 49830266 | 103904176 | KSC-16-283 | S |  | 11±1 | 10±3 |
| S178 | 46873813 | 99313594 | KSC-16-196 | S |  | 1.5±0.2 | 7.1±0.5 |
| <p>* Designates whether a compound was purchased (P) or synthesized (S)</p> <p>[#] Compound identifier used in the main text.</p> | | | | | | | |

Table S11: 3,4-Dihydro-1,4-benzoxazine analogues incorporating the quinazoline of **ML241**

| compound identifiers | | | | |  | p97 inhibition | |
|-------------------------|----------|-----------|------------|---|--|---------------------------------|---|
| Cpd | CID | SID | KU SCC # | * | R4 | ATPase IC ₅₀ (μM) | Ub ^{G76V} GFP IC ₅₀ (μM) |
| S179 40 [#] | 49830256 | 103904182 | KSC-16-261 | S |  | 1.9±0.4 | 3.7±0.6 |

| | | | | | | | |
|-------------------------|----------|-----------|--------------|---|--|---------|---------|
| S180 41 [#] | 49830261 | 103904186 | KSC-16-295 | S |  | 1.2±0.2 | 3±0.6 |
| S181 42 [#] | 49830262 | 103904187 | KSC-16-299 | S |  | 7.4±0.9 | 8.2±1 |
| S182 | 46931214 | 99437736 | KSC-16-219 | S |  | 19±5 | 15±4 |
| S183 43 [#] | 46931210 | 99437737 | KSC-16-222 | S |  | 4.6±1 | 6±0.6 |
| S184 | 46931211 | 99437740 | KSC-16-235c2 | S |  | 2.4±0.5 | 7.3±1 |
| S185 | 46931215 | 99437739 | KSC-16-227 | S |  | 47±22 | 4.5±0.5 |
| S186 | 49830271 | 103904178 | KSC-16-243 | S |  | 52±10 | 19±4 |

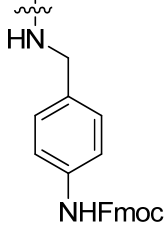
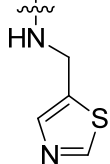
| | | | | | | | |
|---|----------|-----------|------------|---|--|------|------|
| S187 | 49830254 | 103904179 | KSC-16-251 | S |  | 33±7 | 23±2 |
| S188 | 49852170 | 104221951 | KSC-25-6 | S |  | 38±7 | 20±3 |
| <p>* Designates whether a compound was purchased (P) or synthesized (S)</p> <p># Compound identifier used in the main text.</p> | | | | | | | |

Table S12: Unabridged compound purity assessment via HPLC analysis.

| internal compound ID | compound number(s) | HPLC purity (%) ¹ |
|----------------------|--------------------|------------------------------|
| KSC-1-150 | 1, S1 | 100.0 |
| KSC-1-146 | 2, S2 | 100.0 |
| KSC-1-149 | 3, S3 | 94.5 |
| KSC-1-193 | 4, S19 | 99.2 |
| KSC-1-194 | 5, S20 | 99.5 |
| KSC-1-152 | 6, S35 | 92.0 |
| KSC-1-151 | 7, S36 | 100.0 |
| KSC-1-258 | 8, S34 | 100.0 |
| KSC-16-146 | 9, S56 | 98.8 |
| KSC-1-153 | 10, S58 | 99.1 |
| KSC-1-244 | 11, S68 | 96.7 |
| KSC-16-98 | 12, S95 | 100.0 |
| KSC-16-2 | 13, S108 | 96.8 |
| KSC-16-121c | 14, S130 | 98.9 |
| KSC-16-70 | 15, S144 | 99.0 |
| KSC-206-026 | 16 | 96.1 |
| KSC-25-14 | 17, S162 | 95.3 |
| KSC-25-31 | 18, S161 | 81.2 |
| KSC-16-290 | ML241 | 98.3 |
| KSC-16-270 | ML240, S158 | 100.0 |
| KSC-25-21 | 19, S167 | 96.9 |
| KSC-16-187 | 20, S170 | 83.1 |
| KSC-25-40 | 21 | 95.6 |
| KSC-25-23 | 22 | 94.4 |
| KSC-25-38 | 23 | 97.8 |

| | | |
|----------------|-----------------|-------|
| KSC-206-023 | 24 | 95.5 |
| KSC-206-022 | 25 | 93.2 |
| KSC-206-019 | 26 | 90.2 |
| KSC-206-017 | 27 | 98.8 |
| KSC-206-017-P2 | 28 | 96.8 |
| KSC-206-015 | 29 | 99.0 |
| KSC-206-007 | 30 | 98.8 |
| KSC-25-24 | 31, S163 | 100.0 |
| KSC-25-28 | 32, S165 | 100.0 |
| KSC-16-260 | 33, S150 | 100.0 |
| KSC-25-29 | 34, S151 | 98.0 |
| KSC-16-265 | 35, S152 | 68.2 |
| KSC-16-268 | 36, S153 | 92.9 |
| KSC-25-30 | 37, S154 | 100.0 |
| KSC-16-191 | 38, S147 | 100.0 |
| KSC-206-005 | 39, S155 | 96.0 |
| KSC-16-261 | 40, S179 | 98.8 |
| KSC-16-295 | 41, S180 | 96.6 |
| KSC-16-299 | 42, S181 | 95.0 |
| KSC-16-222 | 43, S183 | 100.0 |
| KSC-1-292 | 44, S74 | 100.0 |
| KSC-1-300 | 45, S109 | 97.6 |
| KSC-16-6 | 46, S120 | 99.0 |
| KSC-16-30 | 47, S121 | 100.0 |
| KSC-16-36 | 48, S122 | 100.0 |
| KSC-16-41 | 49, S123 | 99.0 |
| KSC-16-193 | 50, S174 | 98.9 |
| KSC-16-194 | 51, S175 | 100.0 |
| KSC-16-282 | 52, S176 | 100.0 |
| KSC-1-145 | S4 | 100.0 |
| KSC-1-226 | S5 | 100.0 |
| KSC-1-236 | S6 | 100.0 |
| KSC-1-234 | S7 | 94.8 |
| KSC-1-227 | S8 | 98.5 |
| KSC-1-224 | S9 | 100.0 |
| KSC-1-212 | S10 | 92.5 |
| KSC-1-219 | S11 | 96.8 |
| KSC-1-220 | S12 | 95.5 |
| KSC-1-221 | S13 | 97.5 |
| KSC-1-222 | S14 | 100.0 |
| KSC-1-223 | S15 | 98.1 |
| KSC-1-225 | S16 | 100.0 |
| KSC-1-237 | S17 | 98.9 |
| KSC-1-216 | S18 | 100.0 |
| KSC-1-195 | S21 | 99.3 |

| | | |
|------------|------------|-------|
| KSC-1-213 | S22 | 100.0 |
| KSC-1-147 | S23 | 99.1 |
| KSC-1-148 | S24 | 100.0 |
| KSC-1-200 | S25 | 100.0 |
| KSC-1-211 | S26 | 100.0 |
| KSC-1-214 | S27 | 97.7 |
| KSC-1-215 | S28 | 100.0 |
| KSC-1-217 | S29 | 100.0 |
| KSC-1-218 | S30 | 100.0 |
| KSC-1-235 | S31 | 100.0 |
| KSC-1-238 | S32 | 100.0 |
| KSC-1-257 | S33 | 96.6 |
| KSC-1-240 | S37 | 100.0 |
| KSC-1-260 | S38 | 100.0 |
| KSC-1-208 | S39 | 100.0 |
| KSC-1-203 | S40 | 100.0 |
| KSC-1-242 | S41 | 81.2 |
| KSC-1-241 | S42 | 98.2 |
| KSC-1-239 | S43 | 96.1 |
| KSC-1-254 | S44 | 96.5 |
| KSC-16-190 | S45 | 97.7 |
| KSC-16-272 | S46 | 100.0 |
| KSC-16-277 | S47 | 98.6 |
| KSC-25-10 | S48 | 100.0 |
| KSC-25-16 | S49 | 98.2 |
| KSC-16-149 | S50 | 96.2 |
| KSC-16-163 | S51 | 100.0 |
| KSC-16-164 | S52 | 100.0 |
| KSC-16-174 | S53 | 98.4 |
| KSC-16-176 | S54 | 97.8 |
| KSC-16-151 | S55 | 100.0 |
| KSC-1-243 | S57 | 100.0 |
| KSC-1-251 | S59 | 100.0 |
| KSC-1-246 | S60 | 100.0 |
| KSC-1-249 | S61 | 100.0 |
| KSC-1-245 | S62 | 97.7 |
| KSC-1-250 | S63 | 91.5 |
| KSC-1-252 | S64 | 100.0 |
| KSC-1-247 | S65 | 97.7 |
| KSC-1-248 | S66 | 96.1 |
| KSC-1-253 | S67 | 100.0 |
| KSC-1-259 | S69 | 100.0 |
| KSC-1-290 | S70 | 92.1 |
| KSC-1-293 | S71 | 98.5 |
| KSC-1-291 | S72 | 99.0 |

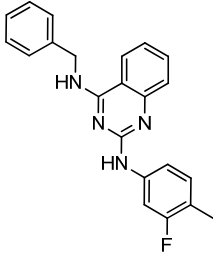
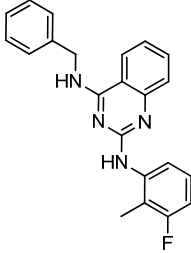
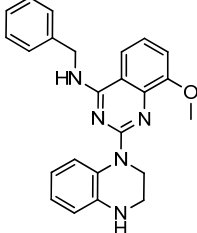
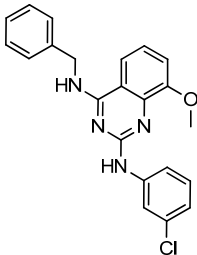
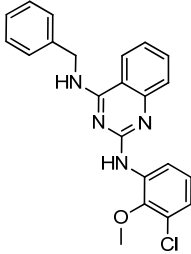
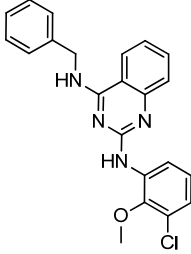
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|------------|-------------|-------|
| KSC-16-155 | S73 | 100.0 |
| KSC-1-295 | S75 | 98.2 |
| KSC-1-294 | S76 | 98.6 |
| KSC-16-103 | S77 | 96.3 |
| KSC-16-104 | S78 | 100.0 |
| KSC-16-105 | S79 | 100.0 |
| KSC-16-106 | S80 | 97.6 |
| KSC-16-107 | S81 | 99.0 |
| KSC-16-108 | S82 | 100.0 |
| KSC-16-109 | S83 | 100.0 |
| KSC-16-110 | S84 | 100.0 |
| KSC-16-112 | S85 | 100.0 |
| KSC-16-113 | S86 | 96.4 |
| KSC-16-120 | S87 | 96.5 |
| KSC-1-288 | S88 | 100.0 |
| KSC-1-289 | S89 | 100.0 |
| KSC-16-150 | S90 | 100.0 |
| KSC-16-152 | S91 | 100.0 |
| KSC-16-188 | S92 | 100.0 |
| KSC-16-72 | S93 | 100.0 |
| KSC-16-89 | S94 | 100.0 |
| KSC-16-101 | S96 | 100.0 |
| KSC-16-79 | S97 | 100.0 |
| KSC-16-63 | S98 | 100.0 |
| KSC-16-84 | S99 | 100.0 |
| KSC-16-92 | S100 | 100.0 |
| KSC-16-99 | S101 | 100.0 |
| KSC-16-75 | S102 | 100.0 |
| KSC-16-66 | S103 | 100.0 |
| KSC-16-87 | S104 | 100.0 |
| KSC-16-95 | S105 | 100.0 |
| KSC-16-100 | S106 | 100.0 |
| KSC-16-78 | S107 | 100.0 |
| KSC-16-38 | S111 | 100.0 |
| KSC-16-42 | S112 | 98.1 |
| KSC-16-8 | S113 | 97.5 |
| KSC-16-31 | S114 | 98.9 |
| KSC-16-35 | S115 | 97.7 |
| KSC-16-40 | S116 | 100.0 |
| KSC-16-29 | S117 | 97.3 |
| KSC-16-28 | S118 | 97.2 |
| KSC-16-32 | S119 | 98.4 |
| KSC-16-33 | S110 | 98.4 |
| KSC-16-3 | S124 | 97.4 |
| KSC-16-4 | S125 | 98.6 |

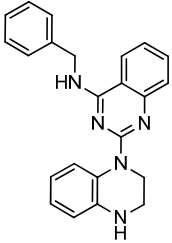
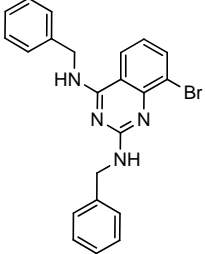
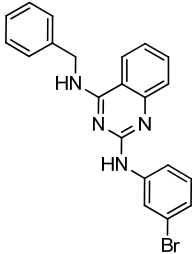
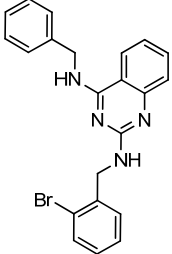
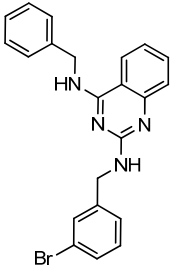
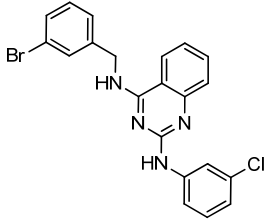
| | | |
|--------------|-------------|-------|
| KSC-16-114 | S126 | 100.0 |
| KSC-16-115 | S127 | 99.0 |
| KSC-16-117 | S128 | 100.0 |
| KSC-16-102 | S129 | 100.0 |
| KSC-16-118 | S131 | 92.0 |
| KSC-16-160c | S132 | 98.6 |
| KSC-16-153 | S133 | 100.0 |
| KSC-16-154 | S134 | 100.0 |
| KSC-16-156 | S135 | 100.0 |
| KSC-16-159 | S136 | 100.0 |
| KSC-16-166 | S137 | 100.0 |
| KSC-16-172 | S138 | 93.2 |
| KSC-16-175 | S139 | 98.0 |
| KSC-16-122 | S140 | 96.8 |
| KSC-16-167c | S141 | 97.5 |
| KSC-16-125 | S142 | 96.1 |
| KSC-16-144 | S143 | 94.8 |
| KSC-16-147 | S145 | 60.6 |
| KSC-16-182 | S146 | 19.5 |
| KSC-16-232 | S148 | 100.0 |
| KSC-16-255 | S149 | 95.6 |
| KSC-25-17 | S156 | 75.0 |
| KSC-25-15c1 | S157 | 96.5 |
| KSC-16-262cc | S159 | 93.9 |
| KSC-25-3 | S160 | 99.2 |
| KSC-25-32 | S164 | 84.4 |
| KSC-25-22 | S166 | 97.9 |
| KSC-25-12 | S168 | 98.8 |
| KSC-25-19 | S169 | 91.1 |
| KSC-16-203 | S171 | 100.0 |
| KSC-16-273 | S172 | 100.0 |
| KSC-16-278 | S173 | 93.5 |
| KSC-16-283 | S177 | 100.0 |
| KSC-16-196 | S178 | 100.0 |
| KSC-16-219 | S182 | 94.9 |
| KSC-16-235c2 | S184 | 95.6 |
| KSC-16-227 | S185 | 91.5 |
| KSC-16-243 | S186 | 81.3 |
| KSC-16-251 | S187 | 97.0 |
| KSC-25-6 | S188 | 98.4 |

¹ Compound purity was measured on the basis of peak integration (area under the curve) from UV/vis absorbance (at 214 nm), and compound identity was determined on the basis of mass analysis.

Table S13: Aqueous solubility for select compounds.

| compound identifiers | | structure | solubility ¹ (µg/mL) pH = 5.0/6.2/7.4 |
|-------------------------|------------|-----------|--|
| cpd | KU SCC # | | |
| S175 51 [#] | KSC-16-294 | | 0.09/<0.01/<0.01 |
| S84 | KSC-16-110 | | 3.4/0.03/0.08 |
| S79 | KSC-16-105 | | 0.05/<0.01/<0.01 |
| S82 | KSC-16-108 | | 5.6/0.07/0.04 |
| S68 11 [#] | KSC-1-244 | | 0.04/0.01/0.02 |
| S144 15 [#] | KSC-16-70 | | 25.2/0.72/0.48 |

| | | | |
|-------------------------|-------------|--|-----------------|
| S-83 | KSC-16-109 |  | 0.13/0.04/0.05 |
| S78 | KSC-16-104 |  | 8.4/0.05/<0.01 |
| S146 | KSC-16-182 |  | 28.2/10.2/0.30 |
| S174 50 [#] | KSC-16-193 |  | 0.08/0.05/<0.01 |
| S77 | KSC-16-103 |  | 0.50/0.23/0.06 |
| S130 14 [#] | KSC-16-121c |  | 3.2/1.0/0.03 |

| | | | |
|-------------------------|------------|--|-----------------|
| S145 | KSC-16-147 |  | >36/18/0.02 |
| S133 | KSC-16-153 |  | 0.42/0.13/<0.01 |
| S71 | KSC-1-293 |  | 0.03/0.01/<0.01 |
| S116 | KSC-16-40 |  | 0.21/0.24/0.14 |
| S123 49 [#] | KSC-16-41 |  | 0.37/0.25/0.17 |
| S106 | KSC-16-100 |  | 0.10/0.02/<0.01 |

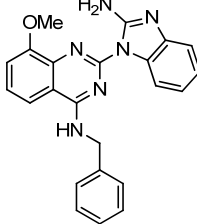
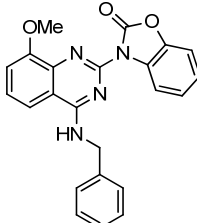
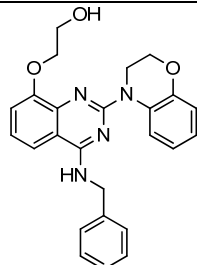
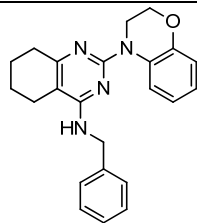
| | | | |
|--|--------------|---|------------------|
| S158 ML240 [#] | KSC-16-270 |  | 0.06/0.09/0.05 |
| S159 | KSC-16-262cc |  | 0.02/<0.01/<0.01 |
| S150 | KSC-16-260 |  | 21.5/0.48/0.43 |
| ML241 [#] | KSC-16-290 |  | 28/0.13/0.20 |
| ¹ in aqueous PION's buffer, pH's 5.0/6.2/7.4 [#] Compound identifier used in the main text. | | | |

Table S14: Kinase/ATPase profiling for ML240 and ML241.

| kinase | annotation | sequence | labeling site | % Inhibition (20 μ M) | |
|-------------------|--|---------------------------|-----------------|------------------------------|--------------|
| | | | | ML240 | ML241 |
| ABL,ARG | Proto-oncogene tyrosine-protein kinase ABL1 [Homo sapiens (Human)] | LMTGDTYTAHAGAKFPIK | Activation Loop | -12.6 | -13.9 |
| ABL,ARG | Proto-oncogene tyrosine-protein kinase ABL1 [Homo sapiens (Human)] | YSLTVAVKTLKEDTMEVEEFLK | Lys1 | 11.1 | 5.3 |
| ACK | Activated CDC42 kinase 1 [Homo sapiens (Human)] | TVSVAVKCLKPDVLSQPEAMDDFIR | Lys1 | 18.9 | -11.3 |
| AGK | Acylglycerol kinase, mitochondrial n=2 Tax=Homo sapiens RepID=AGK_HUMAN | ATVFLNPAACKGK | ATP | 7.5 | 5.2 |
| AMPKa1 | 5'-AMP-activated protein kinase catalytic subunit alpha-1 [Homo sapiens (Human)] | IGHYILGDTLGVGTFGkVK | ATP Loop | 8.3 | 11.5 |
| AMPKa1,A MPKa2 | 5'-AMP-activated protein kinase catalytic subunit alpha-1 [Homo sapiens (Human)] | VAVKILNR | Lys1 | -19.2 | -12.5 |
| AMPKa1,A MPKa2 | 5'-AMP-activated protein kinase catalytic subunit alpha-1 [Homo sapiens (Human)] | DLKPENVLLDAHMINAK | Lys2 | -1.5 | -0.9 |
| AMPKa2 | 5'-AMP-activated protein kinase catalytic subunit alpha-2 [Homo sapiens (Human)] | IGHYVLGDTLGVGTFGkVK | ATP Loop | 11.9 | -6.2 |
| ANPb | Atrial natriuretic peptide receptor B precursor | GMAFLHNSIISSHGSLKSSNCVDSR | Lys2 | 5 | -6.3 |

| | | | | | |
|--------------------------------|--|--------------------------------|-----------------------|-------|-------|
| | [Homo sapiens (Human)] | | | | |
| ARAF | A-Raf proto-oncogene serine/threonine-protein kinase [Homo sapiens (Human)] | DLKSNNIFLHEGLTVK | Lys2 | -7.3 | 3 |
| ATM | Serine-protein kinase ATM [Homo sapiens (Human)] | QLVKGRRDDLQRQDAVMQQVFQMCNTLLQR | ATP | -4.3 | -8.3 |
| ATR | Serine/threonine-protein kinase ATR [Homo sapiens (Human)] | FYIMMCKPK | ATP | -0.4 | -7.4 |
| ATR | Serine/threonine-protein kinase ATR [Homo sapiens (Human)] | KAGHHQTAYNALLNAGESR | Protein Kinase Domain | 1.6 | -7.8 |
| AurA | Serine/threonine-protein kinase 6 [Homo sapiens (Human)] | FILALKVLFK | Lys1 | 10.3 | -1.8 |
| AurA | Serine/threonine-protein kinase 6 [Homo sapiens (Human)] | DIKPENLLGSAGELK | Lys2 | 11.9 | -1 |
| AurB | Serine/threonine-protein kinase 12 [Homo sapiens (Human)] | SHFIVALKVLFK | Lys1 | -32.8 | -14.3 |
| BARK1 | Beta-adrenergic receptor kinase 1 n=1 Tax=Homo sapiens RepID=ARBK1_HUMAN | DLKPANILLDEGHVR | Lys2 | -14.5 | -6.7 |
| BCKDK | [3-methyl-2-oxobutanoate dehydrogenase [lipoamide]] kinase, mitochondrial precursor [Homo sapiens (Human)] | QLDDHKDVVTLAEGLR | Other | -9.9 | -9.4 |
| BRAF | B-Raf proto-oncogene serine/threonine-protein kinase [Homo sapiens (Human)] | DLKSNNIFLHEDLTVK | Lys2 | 10.5 | 14.3 |
| CaMK1a | Calcium/calmodulin-dependent protein kinase type 1 [Homo sapiens (Human)] | LVAIKCIAK | Lys1 | -2.1 | 1.2 |
| CaMK1d | Calcium/calmodulin-dependent protein kinase type 1D [Homo sapiens (Human)] | LFAVKCIPK | Lys1 | 0 | -2.2 |
| CaMK2a, CaMK2b, CaMK2d, CaMK2g | Calcium/calmodulin-dependent protein kinase type II alpha chain [Homo sapiens (Human)] | DLKPENLLLASK | Lys2 | 5.7 | -0.5 |
| CaMK2b, CaMK2d | Calcium/calmodulin-dependent protein kinase type II beta chain [Homo sapiens (Human)] | LCTGHEYAAKIINTK | Lys1 | -1.1 | 12.7 |
| CaMK2d | Calcium/calmodulin-dependent protein kinase type II delta chain n=2 Tax=Euarchontoglires RepID=KCC2D_HUMAN | IP TGQEYAAKIINTK | Lys1 | -14.3 | -17.7 |
| CaMK2g | Calcium/calmodulin-dependent protein kinase type II gamma chain [Homo sapiens (Human)] | KTSTQEYAAKIINTKK | Lys1 | -8.6 | -9.5 |
| CaMK2g | Calcium/calmodulin-dependent protein kinase type II gamma chain [Homo sapiens (Human)] | TSTQEYAAKIINTK | Lys1 | 7.5 | 6.7 |
| CaMKK1 | Calcium/calmodulin-dependent protein kinase kinase 1 [Homo sapiens (Human)] | LAYNESEDRHYAMKVLSK | Lys1 | -24.9 | -7.1 |
| CaMKK2 | Calcium/calmodulin-dependent protein kinase kinase 2 [Homo sapiens (Human)] | LAYNENDNTYYAMKVLSK | Lys1 | -5.8 | 0.1 |
| CASK | Peripheral plasma membrane protein CASK n=2 Tax=Catarrhini RepID=CSKP_HUMAN | ETGQQFAVKIVDVAK | Lys1 | 5.7 | -0.4 |
| CCRK | Cell cycle-related kinase [Homo sapiens (Human)] | DLKPANLLISASGQLK | Lys2 | 2.1 | 4.4 |
| CDC2 | Cell division control protein 2 homolog [Homo sapiens (Human)] | DLKPQNLLIDDKGTIK | Lys2 | -2.6 | -6.5 |
| CDK10 | Cell division protein kinase 10 [Homo sapiens (Human)] | DLKVSNLLMTDK | Lys2 | 4.7 | -7.4 |
| CDK11, CDK8 | Cell division protein kinase 8 [Homo sapiens (Human)] | DLKPANILVMGEGPER | Lys2 | -2.3 | -5.3 |
| CDK2 | Cell division protein kinase 2 [Homo sapiens (Human)] | LTGEVVALKK | Lys1 | -9.5 | -2.8 |
| CDK2 | Cell division protein kinase 2 [Homo sapiens (Human)] | NKLTGEVVALKK | Lys1 | 15.7 | 3.7 |
| CDK2 | Cell division protein kinase 2 [Homo sapiens (Human)] | DLKPQNLLINTEGAIK | Lys2 | -0.8 | -1.9 |
| CDK5 | Cell division protein kinase 5 [Homo sapiens (Human)] | ETHEIVALKR | Lys1 | -20.3 | -10.8 |
| CDK5 | Cell division protein kinase 5 [Homo sapiens (Human)] | NRETHEIVALKR | Lys1 | -17.2 | -18.9 |

| | | | | | |
|-----------|--|-----------------------------|-----------------------|-------|-------|
| CDK5 | Cell division protein kinase 5 [Homo sapiens (Human)] | DLkPQNLLINR | Lys2 | 10.7 | -5.6 |
| CDK7 | Cell division protein kinase 7 [Homo sapiens (Human)] | DLkPNNLLDENGVLK | Lys2 | 2.5 | -1.7 |
| CDK9 | Cell division protein kinase 9 [Homo sapiens (Human)] | DMkAANVLITR | Lys2 | -14.5 | -15.3 |
| CHED | Cell division cycle 2-like protein kinase 5 [Homo sapiens (Human)] | DIkCSNILLNNRGQIK | Lys2 | 17.4 | 2.7 |
| CHK1 | Serine/threonine-protein kinase Chk1 [Homo sapiens (Human)] | LSkGDGLEFK | Other | -4.2 | -3.2 |
| CHK2 | Serine/threonine-protein kinase Chk2 [Homo sapiens (Human)] | VAIKISK | Lys1 | -4.9 | -5.4 |
| CHK2 | Serine/threonine-protein kinase Chk2 [Homo sapiens (Human)] | DLkPENVLLSSQEEDCLIK | Lys2 | 3.1 | 4.2 |
| CK1a | Casein kinase I isoform alpha [Homo sapiens (Human)] | DIkPDNFLMGIGR | Lys2 | 4.9 | -1.4 |
| CK1d,CK1e | Casein kinase I isoform delta [Homo sapiens (Human)] | DVkpDNFLMGLGKK | Lys2 | -1.5 | -4.8 |
| CK2a2 | Casein kinase II subunit alpha' [Homo sapiens (Human)] | DVkpPHNVIMIDHQKQK | Lys2 | -11.7 | -34.4 |
| CLK2 | Dual specificity protein kinase CLK2 [Homo sapiens (Human)] | LTHTDLkPENILFVNSDYELTYNLEK | Lys2 | -12.9 | -5.9 |
| CRK7 | Cell division cycle 2-related protein kinase 7 [Homo sapiens (Human)] | DIkCSNILLNNSGQIK | Lys2 | -31.4 | -22.3 |
| CSK | Tyrosine-protein kinase CSK [Homo sapiens (Human)] | EASSTQDTGkLPVK | Activation Loop | -21.6 | -22 |
| CSK | Tyrosine-protein kinase CSK [Homo sapiens (Human)] | VSDFGLTkEASSTQDTGK | Activation Loop | -10.5 | -1.8 |
| CSK | Tyrosine-protein kinase CSK [Homo sapiens (Human)] | VSDFGLTkEASSTQDTGKLPVK | Activation Loop | -18 | -8.1 |
| DNAPK | DNA-dependent protein kinase catalytic subunit [Homo sapiens (Human)] | GHDEREHPFLVKGGEDLRQDQR | ATP | 12.4 | 1.7 |
| DNAPK | DNA-dependent protein kinase catalytic subunit [Homo sapiens (Human)] | kGGSWIQEINVAEK | ATP | 79.1 | 45.3 |
| eEF2K | Elongation factor 2 kinase [Homo sapiens (Human)] | YIKYNSNSGFVR | Protein Kinase Domain | -5.9 | -1.9 |
| EGFR | Epidermal growth factor receptor precursor [Homo sapiens (Human)] | ITDFGLAKLLGAEEK | Activation Loop | 12.7 | -3.9 |
| EGFR | Epidermal growth factor receptor precursor [Homo sapiens (Human)] | LLGAEEKEYHAEGGKVPK | Activation Loop | 0.1 | -3.2 |
| EGFR | Epidermal growth factor receptor precursor [Homo sapiens (Human)] | IPVAIKELR | Lys1 | 9.7 | -7.4 |
| EphA1 | Ephrin type-A receptor 1 precursor [Homo sapiens (Human)] | LLDDFDGTYETQGGKIPIR | Activation Loop | -22.2 | -26.1 |
| EphA2 | Ephrin type-A receptor 2 precursor [Homo sapiens (Human)] | VLEDDPEATYTTSGGKIPIR | Activation Loop | -8.1 | -9.6 |
| EphA2 | Ephrin type-A receptor 2 precursor [Homo sapiens (Human)] | EVPVAIKTLK | Lys1 | -11.4 | -5.6 |
| EphA7 | Ephrin type-A receptor 7 n=1 Tax=Homo sapiens RepID=EPHA7_HUMAN | VIEDDPEAVYTTTGGkIPVR | Activation Loop | 2.9 | 12 |
| EphB2 | Ephrin type-B receptor 2 precursor [Homo sapiens (Human)] | FLEDDTSDPTYTSALGGKIPIR | Activation Loop | 8.3 | 2.6 |
| EphB4 | Ephrin type-B receptor 4 precursor [Homo sapiens (Human)] | FLEENSSDPTYTSSLGGKIPIR | Activation Loop | -8.8 | -4 |
| Erk1,Erk2 | Mitogen-activated protein kinase 3 [Homo sapiens (Human)] | DLkPSNLLINTTCDLK | Lys2 | 3.6 | 3.5 |
| Erk1,Erk2 | Mitogen-activated protein kinase 3 [Homo sapiens (Human)] | YIHSA NVLHRDLkPSNLLINTTCDLK | Lys2 | -12.2 | 8.6 |
| Erk1,Erk2 | Mitogen-activated protein kinase 1 [Homo sapiens] | YIHSA NVLHRDLkPSNLLINTTCDLK | Lys2 | -10 | 5.3 |
| Erk5 | Mitogen-activated protein kinase 7 n=2 Tax=Homo sapiens RepID=MK07_HUMAN | DLkPSNLLVNENCELK | Lys2 | -14.3 | -6.4 |
| FAK | Focal adhesion kinase 1 [Homo sapiens] | YMEDSTYYKASK | Activation | -20.3 | 6.5 |

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|------------------|--|---|-----------------------|-------|-------|
| | (Human)] | | Loop | | |
| FAK | Focal adhesion kinase 1 [Homo sapiens (Human)] | CIGEGQFGDVHQGIYMSPENPALAVAikTC K | Lys1 | 6.5 | -2 |
| FER | Proto-oncogene tyrosine-protein kinase FER n=2 Tax=Homo sapiens RepID=FER_HUMAN | QEDGGVYSSSGLkQIPIK | Activation Loop | -27.4 | -20.1 |
| FER | Proto-oncogene tyrosine-protein kinase FER n=2 Tax=Homo sapiens RepID=FER_HUMAN | TSVAVKtCKEDLPQELK | Lys1 | 4.8 | -1.8 |
| FRAP | FKBP12-rapamycin complex-associated protein [Homo sapiens (Human)] | IQSIAPSLQVITskQRPR | ATP | 22.6 | -0.2 |
| FYN | Proto-oncogene tyrosine-protein kinase Fyn n=2 Tax=Homo sapiens RepID=FYN_HUMAN | VAIKTLKPGTMSPESFLEEAQIMK | Lys1 | -15.9 | -18 |
| FYN, SRC, YES | Proto-oncogene tyrosine-protein kinase Fyn n=2 Tax=Homo sapiens RepID=FYN_HUMAN | QGAKFPIKWTAPEAALYGR | Activation Loop | 7.4 | 1.5 |
| GCK | Mitogen-activated protein kinase kinase kinase 2 n=1 Tax=Homo sapiens RepID=M4K2_HUMAN | DTVTSELAAVkIVK | Lys1 | 6.7 | 5 |
| GCK | Mitogen-activated protein kinase kinase kinase 2 n=1 Tax=Homo sapiens RepID=M4K2_HUMAN | DIkGANLLTLQGDVK | Lys2 | -34 | -22.6 |
| GCN2 domain2 | Eukaryotic translation initiation factor 2-alpha kinase 4 [Homo sapiens (Human)] | LDGCCYAVkR | Lys1 | -15.1 | -13.9 |
| GCN2 domain2 | Eukaryotic translation initiation factor 2-alpha kinase 4 [Homo sapiens (Human)] | VQNKLDGCCYAVkR | Lys1 | 2.3 | -5.4 |
| GCN2 domain2 | Eukaryotic translation initiation factor 2-alpha kinase 4 [Homo sapiens (Human)] | DLkPVNIFLSDDHVK | Lys2 | 12.6 | 1 |
| GSK3A | Glycogen synthase kinase-3 alpha [Homo sapiens (Human)] | DIkPQNLLVDPDTAVLK | Lys2 | 2 | 0 |
| GSK3B | Glycogen synthase kinase-3 beta n=2 Tax=Homo sapiens RepID=GSK3B_HUMAN | DIkPQNLLDPDTAVLK | Lys2 | 1 | -3.9 |
| HER2/Erb B2 | Receptor tyrosine-protein kinase erbB-2 precursor [Homo sapiens (Human)] | GIWIPDGENVKIPVAikVLR | Lys1 | 32.6 | 0.8 |
| IKKa | Inhibitor of nuclear factor kappa-B kinase alpha subunit [Homo sapiens (Human)] | DLkPENIVLQDVGGK | Lys2 | 8.5 | 10.8 |
| IKKb | Inhibitor of nuclear factor kappa B kinase beta subunit [Homo sapiens (Human)] | DLkPENIVLQQGEQR | Lys2 | -13.4 | -6.4 |
| IKKe, TBK1 | Inhibitor of nuclear factor kappa-B kinase epsilon subunit [Homo sapiens (Human)] | DIkPGNIMR | Lys2 | -6.7 | -9.7 |
| ILK | Integrin-linked protein kinase 1 [Homo sapiens (Human)] | WQGNDIVVkvLK | Lys1 | 1.5 | 0.2 |
| ILK | Integrin-linked protein kinase 1 [Homo sapiens (Human)] | ISMADVkfSFQCPR | Protein Kinase Domain | -2.4 | 1.8 |
| IRAK1 | Interleukin-1 receptor-associated kinase 1 [Homo sapiens (Human)] | AIQFLHQDSPSLIHGDikSSNVLLDER | Lys2 | -2.2 | -2.4 |
| IRAK4 | Interleukin-1 receptor-associated kinase 4 [Homo sapiens (Human)] | GYVNNTTVAVkK | Lys1 | -14.3 | 22.5 |
| IRAK4 | Interleukin-1 receptor-associated kinase 4 [Homo sapiens (Human)] | DIkSANILLDEAFTAK | Lys2 | -23.6 | -7.7 |
| IRE1 | Endoribonuclease n=1 Tax=Homo sapiens RepID=ERN1_HUMAN | DLkPHNILISMPNAHGK | Lys2 | -6.5 | -3.3 |
| ITPK1 | Inositol-tetrakisphosphate 1-kinase [Homo sapiens (Human)] | ESIFFNSHNvSKPESSSVLTeldKIEGVFERP SDEVIR | Other | -7.7 | 4.8 |
| JAK1 domain1 | Tyrosine-protein kinase JAK1 n=1 Tax=Homo sapiens RepID=JAK1_HUMAN | QLASALSYLEDKDLVHGNVCTkNLLAR | Other | 91.8 | 7.1 |
| JAK1 domain2 | Tyrosine-protein kinase JAK1 n=1 Tax=Homo sapiens RepID=JAK1_HUMAN | IGDFGLTkaIETDkEYYTVK | Activation Loop | 1.6 | 0.5 |
| JAK1 domain2 | Tyrosine-protein kinase JAK1 n=1 Tax=Homo sapiens RepID=JAK1_HUMAN | IGDFGLTkaIETDkEYYTVKDDR | Activation Loop | -10.7 | 4.1 |
| JNK1, JNK2, JNK3 | Mitogen-activated protein kinase 8 [Homo sapiens (Human)] | DLkPSNIVVK | Lys2 | 9.6 | -7 |
| KHS1 | Mitogen-activated protein kinase kinase kinase 5 [Homo sapiens (Human)] | NVHTGELAAVkiIK | Lys1 | -6.4 | -7.4 |
| KHS2 | Mitogen-activated protein kinase kinase kinase 3 [Homo sapiens (Human)] | NVNTGELAAikVIK | Lys1 | 4.8 | 3.3 |

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|------------------------|---|--|-----------------|-------|-------|
| LATS1 | Serine/threonine-protein kinase LATS1 [Homo sapiens (Human)] | ALYATKTLR | Lys1 | -30.5 | -8 |
| LATS2 | Serine/threonine-protein kinase LATS2 n=1 Tax=Homo sapiens ReplD=LATS2_HUMAN | VDTHALYAMkTLR | Lys1 | 11.4 | 6.1 |
| LATS2 | Serine/threonine-protein kinase LATS2 n=1 Tax=Homo sapiens ReplD=LATS2_HUMAN | DIKPDNILDLDGHIK | Lys2 | -0.2 | -3.7 |
| LKB1 | Serine/threonine-protein kinase 11 [Homo sapiens (Human)] | DIKPGNLLLTGGTLK | Lys2 | 4.4 | -3 |
| LKB1 | Serine/threonine-protein kinase 11 [Homo sapiens (Human)] | FPVCQAHGYFCQLIDGLEYLHSQGIVHKDI KPGNLLLTGGTLK | Lys2 | -8.8 | 25.7 |
| LOK | Serine/threonine-protein kinase 10 [Homo sapiens (Human)] | NKETGALAAAKVIETK | Lys1 | 7.4 | 9.5 |
| LOK | Serine/threonine-protein kinase 10 [Homo sapiens (Human)] | DLKAGNVLMTLEGDIR | Lys2 | -9.3 | -7.7 |
| LYN | Tyrosine-protein kinase Lyn n=1 Tax=Homo sapiens ReplD=LYN_HUMAN | VAVkTLKPGTMSVQAFLEEANLMK | Lys1 | -9.1 | -1.4 |
| MAP2K1, MAP2K2 | Dual specificity mitogen-activated protein kinase kinase 1 n=4 Tax=Eutheria ReplD=MP2K1_HUMAN | DVkpSNILVNSR | Lys2 | -17.1 | -3.5 |
| MAP2K3 | Dual specificity mitogen-activated protein kinase kinase 3 [Homo sapiens (Human)] | MCDFGISGYLVDSVAKTMDAGCKPYMAP ER | Activation Loop | 0.7 | 12 |
| MAP2K3 | Dual specificity mitogen-activated protein kinase kinase 3 [Homo sapiens (Human)] | HAQSGTIMAVkR | Lys1 | -4 | -7.2 |
| MAP2K3 | Dual specificity mitogen-activated protein kinase kinase 3 [Homo sapiens (Human)] | DVkpSNVLINK | Lys2 | -13.7 | -10.5 |
| MAP2K4 | Dual specificity mitogen-activated protein kinase kinase 4 [Homo sapiens (Human)] | LCDFGISGQLVDSIAKTR | Activation Loop | -24.7 | 1.6 |
| MAP2K4 | Dual specificity mitogen-activated protein kinase kinase 4 [Homo sapiens (Human)] | MVHKPSGQIMAVkR | Lys1 | -13 | -16.1 |
| MAP2K4 | Dual specificity mitogen-activated protein kinase kinase 4 [Homo sapiens (Human)] | DIkPSNILLDR | Lys2 | 1.9 | -5.2 |
| MAP2K5 | Dual specificity mitogen-activated protein kinase kinase 5 n=1 Tax=Homo sapiens ReplD=MP2K5_HUMAN | DVkpSNMLVNTR | Lys2 | 6.7 | -10.4 |
| MAP2K6 | Dual specificity mitogen-activated protein kinase kinase 6 [Homo sapiens (Human)] | MCDFGISGYLVDSVAKTIDAGCKPYMAPE R | Activation Loop | 2.4 | 3.6 |
| MAP2K6 | Dual specificity mitogen-activated protein kinase kinase 6 [Homo sapiens (Human)] | HVPSGQIMAVkR | Lys1 | 0.1 | -8 |
| MAP2K6 | Dual specificity mitogen-activated protein kinase kinase 6 [Homo sapiens (Human)] | DVkpSNVLINALGQVK | Lys2 | -11.4 | -5.5 |
| MAP3K2 | Mitogen-activated protein kinase kinase 2 n=3 Tax=Homo sapiens ReplD=M3K2_HUMAN | ELAVkQVQFDPDPSPETSKEVNALECEIQLLK | Lys1 | -4.9 | 1.7 |
| MAP3K2 | Mitogen-activated protein kinase kinase 2 n=3 Tax=Homo sapiens ReplD=M3K2_HUMAN | VYLCYDVTGRELAVkQVQFDPDPSPETSKE VNALECEIQLLK | Lys1 | 3.1 | 13.4 |
| MAP3K2, MAP3K3 | Mitogen-activated protein kinase kinase 2 n=3 Tax=Homo sapiens ReplD=M3K2_HUMAN | DIKGANILR | Lys2 | -11.3 | -4.2 |
| MAP3K3 | Mitogen-activated protein kinase kinase 3 n=2 Tax=Homo sapiens ReplD=M3K3_HUMAN | ELASkQVQFDPDPSPETSKEVSALECEIQLLK | Lys1 | -12.9 | -13.5 |
| MAP3K4 | Mitogen-activated protein kinase kinase 4 [Homo sapiens (Human)] | VYTCISVDTGELMAMkEIR | Lys1 | -6.6 | 1.4 |
| MAP3K4 | Mitogen-activated protein kinase kinase 4 [Homo sapiens (Human)] | DIKGANIFLTSSGLIK | Lys2 | -29.3 | -7.7 |
| MAP3K5 | Mitogen-activated protein kinase kinase 5 [Homo sapiens (Human)] | DIKGDNVLINTYSGVLK | Lys2 | -7.6 | -10.3 |
| MAP3K5, MAP3K6, MAP3K7 | Mitogen-activated protein kinase kinase 5 [Homo sapiens (Human)] | IAIkEIPER | Lys1 | -2.3 | -2.8 |
| MAP3K7, TAK1 | Mitogen-activated protein kinase kinase 7 [Homo sapiens (Human)] | DLkPPNLLLVAGGTVLK | Lys2 | -6.3 | -10.3 |
| MAPKAPK | MAP kinase-activated protein kinase 3 [Homo sapiens (Human)] | KYAVTDDYQLSKQVLGLGVNGK | ATP Loop | -7.4 | -11.1 |

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|-------------------|--|---------------------------------------|-----------------|-------|-------|
| 3 | sapiens (Human)] | | | | |
| MARK2 | Serine/threonine-protein kinase MARK2 [Homo sapiens (Human)] | EVAVKIIDKTLNSSSLQK | Lys1 | -7.2 | -11.2 |
| MARK2,MARK3 | MAP/microtubule affinity-regulating kinase 3 [Homo sapiens (Human)] | DLKAENLLLDADMNIK | Lys2 | -26.2 | -16.4 |
| MARK3 | MAP/microtubule affinity-regulating kinase 3 [Homo sapiens (Human)] | EVAIKIIDKTLNPTSLQK | Lys1 | -1 | 3 |
| MARK3,MARK4 | MAP/microtubule affinity-regulating kinase 3 [Homo sapiens (Human)] | EVAIKIIDK | Lys1 | -5.4 | -7.1 |
| MAST1,MAST2 | Microtubule-associated serine/threonine-protein kinase 2 [Homo sapiens (Human)] | DLKPDNLLITSMGHIK | Lys2 | 5 | 6.4 |
| MAST2,MAST4 | Microtubule-associated serine/threonine-protein kinase 2 [Homo sapiens (Human)] | DLKPDNLLVTSMGHIK | Lys2 | -5.1 | 0.9 |
| MAST3 | Microtubule-associated serine/threonine-protein kinase 3 [Homo sapiens (Human)] | DLKPDNLLITSLGHIK | Lys2 | -8.5 | -6.1 |
| MASTL | Microtubule-associated serine/threonine-protein kinase-like [Homo sapiens (Human)] | GAFGKVYLQK | ATP Loop | -20.9 | -27 |
| MET | Hepatocyte growth factor receptor precursor [Homo sapiens (Human)] | DMYDKEYYSVHNK | Activation Loop | -27 | -4.2 |
| MET | Hepatocyte growth factor receptor precursor [Homo sapiens (Human)] | DMYDKEYYSVHNKGTAK | Activation Loop | -15 | -7 |
| MLK1 | Mitogen-activated protein kinase kinase kinase 9 n=1 Tax=Homo sapiens RepID=M3K9_HUMAN | DLKSSNILLQK | Lys2 | 11.3 | 3.8 |
| MLK2 | Mitogen-activated protein kinase kinase kinase 10 n=1 Tax=Homo sapiens RepID=M3K10_HUMAN | DLKSINILILEAIENHNLDTVLK | Lys2 | 17.4 | 14.1 |
| MLK3 | Mitogen-activated protein kinase kinase kinase 11 [Homo sapiens (Human)] | EWHKTTQMSAAGTYAWMAPEVIK | Activation Loop | 14.3 | 10.5 |
| MLK3 | Mitogen-activated protein kinase kinase kinase 11 [Homo sapiens (Human)] | DLKSNNILLQPIESDDMEHK | Lys2 | 3.9 | 4.1 |
| MLK4 | Mitogen-activated protein kinase kinase kinase [Homo sapiens (Human)] | DLKSSNILLEK | Lys2 | 14.6 | -6 |
| MLKL | CDNA FLJ34389 fis, clone HCHON2000087 [Homo sapiens (Human)] | APVAIKVFK | Lys1 | -10.7 | -9.3 |
| MPSK1 | Serine/threonine-protein kinase 16 n=1 Tax=Homo sapiens RepID=STK16_HUMAN | LGEGGFSYVDLVEGLHDGHFYALKR | Lys1 | 2.9 | 6 |
| MPSK1 | Serine/threonine-protein kinase 16 n=1 Tax=Homo sapiens RepID=STK16_HUMAN | DLKPTNILLGDEGQPVLMDLGSMNQACIHVEGSR | Lys2 | -11.7 | -1.7 |
| MRCKb | Serine/threonine-protein kinase MRCK beta n=1 Tax=Homo sapiens RepID=MRCKB_HUMAN | DIKPDNVLLDVNGHIR | Lys2 | -1.3 | -0.5 |
| MRCKb | Serine/threonine-protein kinase MRCK beta n=1 Tax=Homo sapiens RepID=MRCKB_HUMAN | NHHVHLYPWSSLDGAEGSFDIKLPETK | Other | 1.2 | 5.1 |
| MSK1 domain1 | Ribosomal protein S6 kinase alpha 5 [Homo sapiens (Human)] | DIKLENILLDSNGHVVLTDGFLSK | Lys2 | 1 | -0.8 |
| MSK1 domain1 | Ribosomal protein S6 kinase alpha 5 [Homo sapiens (Human)] | LGIIYRDIKLENILLDSNGHVVLTDGFLSK | Lys2 | 8.5 | 10.9 |
| MSK1,MSK2 domain1 | Ribosomal protein S6 kinase alpha 5 [Homo sapiens (Human)] | VLGTGAYGKVFLVR | ATP Loop | 2.9 | 1.4 |
| MSK2 domain1 | Ribosomal protein S6 kinase alpha 4 [Homo sapiens (Human)] | DLKLENVLLDSEGHIVLTDGFLSK | Lys2 | 7.3 | 2.6 |
| MST1 | Serine/threonine-protein kinase 4 [Homo sapiens (Human)] | ETGQIVAIKQVPVESDLQEIIK | Lys1 | 6.2 | 1.2 |
| MST1,MST2 | Serine/threonine-protein kinase 4 [Homo sapiens (Human)] | DIKAGNILLNTEGHAK | Lys2 | -3 | -2.4 |
| MST2 | Serine/threonine-protein kinase 3 [Homo sapiens (Human)] | ESGQVVAIKQVPVESDLQEIIK | Lys1 | -5.8 | -3.6 |
| MST2 | Serine/threonine-protein kinase 3 [Homo sapiens (Human)] | ESGQVVAIKQVPVESDLQEIIKEISIMQQCDSPYVVK | Lys1 | -32 | -8.3 |
| MST3 | Serine/threonine-protein kinase 24 [Homo sapiens (Human)] | DIKAANVLLSEHGEVK | Lys2 | -9.9 | -7 |

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| MST4 | Serine/threonine-protein kinase MST4 [Homo sapiens (Human)] | TQQVVAIKIIDLEEADEIEDIQEITVLSQC DSSVYTK | Lys1 | 31.1 | 38.2 |
| MST4,YSK 1 | Serine/threonine-protein kinase 25 [Homo sapiens (Human)] | DIkAANVLLSEQGDVK | Lys2 | -30.2 | -15.5 |
| NDR1 | Serine/threonine-protein kinase 38 [Homo sapiens (Human)] | DTGHVYAMkILR | Lys1 | -9.4 | -10.8 |
| NDR2 | Serine/threonine-protein kinase 38-like [Homo sapiens (Human)] | DTGHIYAMkILR | Lys1 | 4.2 | -6.5 |
| NDR2 | Serine/threonine-protein kinase 38-like [Homo sapiens (Human)] | DIkPDNLLLDK | Lys2 | -11.8 | -8 |
| NEK1 | Serine/threonine-protein kinase Nek1 [Homo sapiens (Human)] | DIkSQNIFLTK | Lys2 | -13 | -7.6 |
| NEK3 | Serine/threonine-protein kinase Nek3 [Homo sapiens (Human)] | SkNIFLTQNGK | Activation Loop | 2.9 | 5.9 |
| NEK4 | Serine/threonine-protein kinase Nek4 [Homo sapiens (Human)] | DLkTQNVFLTR | Lys2 | -7.4 | -18.5 |
| NEK6,NEK 7 | Serine/threonine-protein kinase Nek6 [Homo sapiens (Human)] | DIkPANVFITATGVVK | Lys2 | 6.1 | -4.4 |
| NEK7 | Serine/threonine-protein kinase Nek7 [Homo sapiens (Human)] | AACLLDGVPVAlkK | Lys1 | -1 | -6 |
| NEK8 | Serine/threonine-protein kinase Nek8 [Homo sapiens (Human)] | DLkTQNILLDK | Lys2 | -12.2 | -15.9 |
| NEK9 | Serine/threonine-protein kinase Nek9 n=1 Tax=Homo sapiens RepID=NEK9_HUMAN | LG DYGLAKK | Activation Loop | -22.1 | -12.3 |
| NEK9 | Serine/threonine-protein kinase Nek9 n=1 Tax=Homo sapiens RepID=NEK9_HUMAN | TEDDSL VVWKEVDLTR | Lys1 | -9.3 | 5 |
| NEK9 | Serine/threonine-protein kinase Nek9 n=1 Tax=Homo sapiens RepID=NEK9_HUMAN | DIkTLNIFLTK | Lys2 | -5.8 | 1.1 |
| OSR1 | Serine/threonine-protein kinase OSR1 [Homo sapiens (Human)] | DV kAGNILLGEDGSVQIADFGVSAFLATGG DITR | Lys2 | -6.6 | -9 |
| p38a | Mitogen-activated protein kinase 14 n=3 Tax=Eutheria RepID=MK14_HUMAN | DLkPSNLAVNEDCElK | Lys2 | 16.5 | 6.3 |
| p38a | Mitogen-activated protein kinase 14 n=3 Tax=Eutheria RepID=MK14_HUMAN | QELNkTIWEVPER | Other | -2.1 | -5.7 |
| p38b | Mitogen-activated protein kinase 11 n=2 Tax=Homo sapiens RepID=MK11_HUMAN | QELNkTVWEVPQR | Other | -9.6 | -9.7 |
| p38d,p38g | Mitogen-activated protein kinase 12 [Homo sapiens (Human)] | DLkPGNLAVNEDCElK | Lys2 | -11.1 | 2.8 |
| p70S6K | Ribosomal protein S6 kinase 1 (EC 2.7.1.37) (S6K) (S6K1) (70 kDa ribosomal protein S6 kinase 1) (p70 S6 kinase alpha) (p70(S6K)-alpha) [Homo sapiens (Human)] | LTD FGLCKESIHDGTVTHTFCGTIEYMAPEI LMR | Activation Loop | -15.5 | -8.4 |
| p70S6K | Ribosomal protein S6 kinase 1 (EC 2.7.1.37) (S6K) (S6K1) (70 kDa ribosomal protein S6 kinase 1) (p70 S6 kinase alpha) (p70(S6K)-alpha) [Homo sapiens (Human)] | DLkPENIMLNHQGHVK | Lys2 | -6.9 | -6.4 |
| p70S6K,p7 0S6Kb | Ribosomal protein S6 kinase 1 (EC 2.7.1.37) (S6K) (S6K1) (70 kDa ribosomal protein S6 kinase 1) (p70 S6 kinase alpha) (p70(S6K)-alpha) [Homo sapiens (Human)] | GGYGkVFQVR | ATP Loop | -2.3 | 0.8 |
| PCTAIRE1 | Serine/threonine-protein kinase PCTAIRE-1 [Homo sapiens (Human)] | LTDNLVALKEIR | Lys1 | -2.7 | 2.9 |
| PCTAIRE2 | Serine/threonine-protein kinase PCTAIRE-2 [Homo sapiens (Human)] | DLkPQNLLINEK | Lys2 | -40.2 | -12.4 |
| PCTAIRE2, PCTAIRE3 | Serine/threonine-protein kinase PCTAIRE-2 [Homo sapiens (Human)] | SKLTENLVALKEIR | Lys1 | 10.3 | -1.8 |
| PDHK1 | [Pyruvate dehydrogenase [lipoamide]] kinase isozyme 1, mitochondrial precursor [Homo sapiens (Human)] | SPGQPIQVVYVPSHLYHMFELFKNAMR | Other | 31.4 | 16.9 |
| PDK1 | 3-phosphoinositide-dependent protein kinase 1 [Homo sapiens (Human)] | EYAIkILEK | Lys1 | -5.3 | -11.8 |
| PEK | Eukaryotic translation initiation factor 2-alpha kinase 3 precursor [Homo sapiens (Human)] | DLkPSNIFFTMDDEVVK | Lys2 | -7.4 | -3.9 |
| PFTAIRE1 | Serine/threonine-protein kinase PFTAIRE-1 | LVALkVIR | Lys1 | 8.2 | -4.9 |

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|---------------|--|--|------|-------|-------|
| | n=1 Tax=Homo sapiens RepID=PFTK1_HUMAN | | | | |
| PFTAI1RE1 | Serine/threonine-protein kinase PFTAI1RE-1 n=1 Tax=Homo sapiens RepID=PFTK1_HUMAN | DLKPQNLLISDTGELK | Lys2 | -0.6 | -6.5 |
| PHKg1 | Phosphorylase b kinase gamma catalytic chain, skeletal muscle isoform n=2 Tax=Homo sapiens RepID=PHKG1_HUMAN | DLKPENILLDDNMNIK | Lys2 | 6.1 | 2 |
| PHKg2 | Phosphorylase b kinase gamma catalytic chain, testis/liver isoform [Homo sapiens (Human)] | ATGHEFAVKIMEVTAER | Lys1 | 4.6 | -2.7 |
| PI4KA,PI4KAP2 | Phosphatidylinositol 4-kinase alpha n=2 Tax=Homo sapiens RepID=PI4KA_HUMAN | SGTPMQSAAKAPYLAK | ATP | -7.4 | -3.1 |
| PI4KB | Phosphatidylinositol 4-kinase beta n=2 Tax=Homo sapiens RepID=PI4KB_HUMAN | VPHTQAVVLNSKDK | ATP | 2 | -16.5 |
| PI4KB | Phosphatidylinositol 4-kinase beta n=2 Tax=Homo sapiens RepID=PI4KB_HUMAN | VPHTQAVVLNSKDKAPYLIYVEVLECFD TTSVPAR | ATP | 9.8 | -5.8 |
| PIK3C2B | Phosphatidylinositol-4-phosphate 3-kinase C2 domain-containing beta polypeptide [Homo sapiens] | VIFKCGDDLRLQDMLTLQMIR | ATP | 52.1 | 40.3 |
| PIK3C3 | Phosphatidylinositol 3-kinase catalytic subunit type 3 [Homo sapiens (Human)] | TEDGGKYPVIFKHGDDLRL | ATP | 1.8 | -16.5 |
| PIK3C3 | Phosphatidylinositol 3-kinase catalytic subunit type 3 [Homo sapiens (Human)] | TEDGGKYPVIFKHGDDLRLQDQLILQIISLM DK | ATP | 13.7 | 14.3 |
| PIK3CA | Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha isoform n=2 Tax=Homo sapiens RepID=PK3CA_HUMAN | RPLWLNWENPDIMSELLFQNNIEIFKNGD DLRQDMLTLQIIR | ATP | 5.6 | 28.5 |
| PIK3CB | Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta isoform [Homo sapiens (Human)] | VFGEDSVGVIFKNGDDLRL | ATP | 5.6 | -9 |
| PIK3CB | Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit beta isoform [Homo sapiens (Human)] | VFGEDSVGVIFKNGDDLRLQDMLTLQMLR | ATP | 0.9 | 6.7 |
| PIP4K2A | Phosphatidylinositol-4-phosphate 5-kinase type II alpha (EC 2.7.1.68) (1-phosphatidylinositol-4-phosphate 5-kinase 2-alpha) (PtdIns(4)P-5-kinase isoform 2-alpha) (PIP5KI-alpha) (Diphosphoinositide kinase 2-alpha) (PtdIns(4)P-5-kinase B isoform) (PIP5KI | AKELPTLKDNDFINEGQK | ATP | 0.5 | -4.5 |
| PIP4K2B | Phosphatidylinositol-4-phosphate 5-kinase type II beta (EC 2.7.1.68) (1-phosphatidylinositol-4-phosphate 5-kinase 2-beta) (PtdIns(4)P-5-kinase isoform 2-beta) [Homo sapiens (Human)] | DLPTFKDNDFLNEGQK | ATP | -4.7 | 15.9 |
| PIP4K2C | Phosphatidylinositol-5-phosphate 4-kinase type-2 gamma n=1 Tax=Homo sapiens RepID=PI42C_HUMAN | ELPTLKDMDFLNK | ATP | -8.2 | -6.7 |
| PIP4K2C | Phosphatidylinositol-5-phosphate 4-kinase type-2 gamma n=1 Tax=Homo sapiens RepID=PI42C_HUMAN | TLVIKEVSSEDIADMHSNLSNYHQYIVK | ATP | -9.4 | -10.9 |
| PIP4K2C | Phosphatidylinositol-5-phosphate 4-kinase type-2 gamma n=1 Tax=Homo sapiens RepID=PI42C_HUMAN | VKELPTLKDMDFLNK | ATP | 16 | 4.2 |
| PIP5K3 | FYVE finger-containing phosphoinositide kinase (EC 2.7.1.68) (1-phosphatidylinositol-4-phosphate 5-kinase) (Phosphatidylinositol-3-phosphate 5-kinase type III) (PIP5K) (PtdIns(4)P-5-kinase) [Homo sapiens (Human)] | GGKSGAAFYATEDDRFILK | ATP | 96.6 | -7.7 |
| PITSLRE | PITSLRE serine/threonine-protein kinase CDC2L1 [Homo sapiens (Human)] | DLKTSNLLSHAGILK | Lys2 | 4.6 | -1.1 |
| PKCa,PKCb | Protein kinase C alpha type n=2 Tax=Homo sapiens RepID=KPCA_HUMAN | DLKLDNVMLDSEGHK | Lys2 | -0.1 | -1.9 |
| PKCi | Protein kinase C iota type [Homo sapiens (Human)] | IYAMkVVK | Lys1 | -13.3 | -0.4 |
| PKCz | Protein kinase C zeta type [Homo sapiens (Human)] | NDQIYAMkVVK | Lys1 | 19.7 | 17.3 |
| PKD1 | Serine/threonine-protein kinase D1 n=1 | DVAIKIIDK | Lys1 | -20.7 | -8.8 |

| | | | | | |
|------------------------|--|---|-----------------------|-------|-------|
| | Tax=Homo sapiens RepID=KPCD1_HUMAN | | | | |
| PKD1,PKD2 | Serine/threonine-protein kinase D1 n=1 Tax=Homo sapiens RepID=KPCD1_HUMAN | NIVHCDLKPENVLLASADPFQVK | Lys2 | -10.6 | 5.2 |
| PKD2 | Protein kinase D2 [Homo sapiens (Human)] | DVAVKVIDK | Lys1 | -4.3 | -7.2 |
| PKD3 | Protein kinase D3 [Homo sapiens (Human)] | NIVHCDLKPENVLLASAEPFQVK | Lys2 | -8.9 | 2.8 |
| PKN1 | Protein kinase N1 [Homo sapiens (Human)] | VLLSEFRPSGELFAIKALK | Lys1 | 0.9 | 1.6 |
| PKN2 | Protein kinase N2 [Homo sapiens (Human)] | DLKLDNLLDTEGFVK | Lys2 | -3.6 | 9.1 |
| PKR | Interferon-induced, double-stranded RNA-activated protein kinase [Homo sapiens (Human)] | DLKPSNIFLVDTK | Lys2 | -0.3 | -5.4 |
| PLK1 | Serine/threonine-protein kinase PLK1 [Homo sapiens (Human)] | CFEISDADTKEVFAGKIVPK | Lys1 | -11.4 | -1.5 |
| PLK1 | Serine/threonine-protein kinase PLK1 [Homo sapiens (Human)] | DLKLGNNFLNEDLEVK | Lys2 | -15.2 | -7.2 |
| PRP4 | Serine/threonine-protein kinase PRP4 homolog [Homo sapiens (Human)] | CNIIHADIKPDNIVNESK | Lys2 | -1.8 | -6.7 |
| PRPK | TP53-regulating kinase [Homo sapiens (Human)] | FLSGLELVKQGAER | ATP Loop | 3.2 | 0.3 |
| RIPK2 | Receptor-interacting serine/threonine-protein kinase 2 [Homo sapiens (Human)] | VQVAVKHLHIHTPLDSEK | Lys1 | 7.6 | 0 |
| RIPK2 | Receptor-interacting serine/threonine-protein kinase 2 [Homo sapiens (Human)] | ILHEIALGVNYLHNMTPLLHHDLTQNIL DNEFHVK | Lys2 | 8.8 | 5.3 |
| ROCK1 | Rho-associated protein kinase 1 [Homo sapiens (Human)] | kLQLELNQER | Other | 2.2 | 3.9 |
| ROCK1,ROCK2 | Rho-associated protein kinase 2 [Homo sapiens (Human)] | DVkpDNMLLDK | Lys2 | -22.5 | -16.1 |
| RON | Macrophage-stimulating protein receptor precursor (EC 2.7.1.112) (MSP receptor) (p185-Ron) (CDw136 antigen) [Contains: Macrophage-stimulating protein receptor alpha chain; Macrophage-stimulating protein receptor beta chain] [Homo sapiens (Human)] | IQCAIKSLSR | Lys1 | -13.2 | -10.5 |
| RSK1 domain2 | Ribosomal protein S6 kinase alpha 1 [Homo sapiens (Human)] | DLKPSNIIYVDESGNPECLR | Lys2 | 1 | -6.9 |
| RSK1,RSK2 domain1 | Ribosomal protein S6 kinase alpha 1 [Homo sapiens (Human)] | DLKPENILLDEEGHIKLTDFGLSK | Lys2 | -1 | 2.1 |
| RSK1,RSK2,RSK3 domain1 | Ribosomal protein S6 kinase alpha 1 [Homo sapiens (Human)] | DLKPENILLDEEGHIK | Lys2 | 8.4 | -2 |
| RSK1,RSK3 | Ribosomal protein S6 kinase alpha 1 [Homo sapiens (Human)] | SkRDPSEEIEILLR | Other | 2.1 | 1.5 |
| RSK1,RSK4 domain1 | Ribosomal protein S6 kinase alpha 1 [Homo sapiens (Human)] | VLGQGSFGKVFVLR | ATP Loop | 9 | -10.3 |
| RSK2 domain1 | Ribosomal protein S6 kinase alpha 3 [Homo sapiens (Human)] | VLGQGSFGKVFVVK | ATP Loop | 34.2 | 3.3 |
| RSK2 domain2 | Ribosomal protein S6 kinase alpha 3 [Homo sapiens (Human)] | DLKPSNIIYVDESGNPESIR | Lys2 | -3.8 | -9.6 |
| RSK2 domain2 | Ribosomal protein S6 kinase alpha 3 [Homo sapiens (Human)] | SkRDPTEEIEILLR | Protein Kinase Domain | 13.3 | 8.5 |
| RSK4 domain1 | Ribosomal protein S6 kinase alpha 6 [Homo sapiens (Human)] | DLKPENILLDEIGHIK | Lys2 | 52.8 | 0.9 |
| RSKL1 domain1 | Ribosomal protein S6 kinase delta-1 n=2 Tax=Homo sapiens RepID=KS6C1_HUMAN | VLGVIDKVLVMDTR | Protein Kinase Domain | 1.1 | -2.6 |
| SGK3 | Serine/threonine-protein kinase Sgk3 [Homo sapiens (Human)] | FYAVKVLQK | Lys1 | -7.6 | -9 |
| SLK | CTCL tumor antigen se20-9 [Homo sapiens (Human)] | ETSVLAAAKVIDTK | Lys1 | -11.1 | -1.8 |
| SLK | CTCL tumor antigen se20-9 [Homo sapiens (Human)] | DLKAGNIFLTLDGDIK | Lys2 | -9.2 | -8.1 |
| SMG1 | Serine/threonine-protein kinase SMG1 n=4 Tax=Homo sapiens RepID=SMG1_HUMAN | DTVTIHVSFGGTITILPTKTKPK | ATP | -5.7 | -7.5 |
| SNRK | SNF-related serine/threonine-protein kinase | DLKPENVVFEK | Lys2 | 1.2 | 0.3 |

| | | | | | |
|-----------------------------|---|-------------------------------------|-----------------|-------|-------|
| | [Homo sapiens (Human)] | | | | |
| SRC | Proto-oncogene tyrosine-protein kinase Src n=1 Tax=Homo sapiens RepID=SRC_HUMAN | VAIKTLKPGTMSPEAFLEQAQVMK | Lys1 | -15.5 | -13.5 |
| SRPK1 | Serine/threonine-protein kinase SRPK1 n=1 Tax=Homo sapiens RepID=SRPK1_HUMAN | IIHTDikPENILLSVNEQYIR | Lys2 | 5.7 | 4.3 |
| SRPK1,SRP K2 | Serine/threonine-protein kinase SRPK1 n=1 Tax=Homo sapiens RepID=SRPK1_HUMAN | FVAMkVVK | Lys1 | -61.9 | -6.3 |
| STLK5 | STE20-related adaptor protein [Homo sapiens (Human)] | YSVKVLPWLSPEVLQQNLQGYDAK | Activation Loop | 5.3 | 10.7 |
| STLK5 | STE20-related adaptor protein [Homo sapiens (Human)] | SVkASHILISVDGK | Lys2 | -32.7 | -5.5 |
| STLK6 | Serine/threonine-protein kinase ALS2CR2 [Homo sapiens (Human)] | HTPTGTLVTikITNLENCNEER | Lys1 | 0.6 | -13.2 |
| STLK6 | Serine/threonine-protein kinase ALS2CR2 [Homo sapiens (Human)] | SIKASHILISGDGLVTLGSLSHLSLVK | Lys2 | -11.4 | 4 |
| TAO1,TAO 3 | Serine/threonine-protein kinase TAO3 [Homo sapiens (Human)] | DIKAGNILLTEPGQVK | Lys2 | -7 | -11.1 |
| TAO2 | Serine/threonine-protein kinase TAO2 n=2 Tax=Homo sapiens RepID=TAOK2_HUMAN | DVKAGNILLSEPGLVK | Lys2 | -6.8 | -2.6 |
| TBK1 | Serine/threonine-protein kinase TBK1 [Homo sapiens (Human)] | TGDLFAIKVFNNISFLRPVDVQMR | Lys1 | -11.4 | 3.3 |
| TLK1 | Serine/threonine-protein kinase tousled-like 1 [Homo sapiens (Human)] | YAAVKIHQLNK | Lys1 | -28.7 | -24.9 |
| TLK1,TLK2 | Serine/threonine-protein kinase tousled-like 1 [Homo sapiens (Human)] | YLNEIKPPIHYDLkPGNILLVDGTACGEIK | Lys2 | 0.3 | -4.7 |
| TLK2 | Serine/threonine-protein kinase tousled-like 2 [Homo sapiens (Human)] | YVAVKIHLNK | Lys1 | -7.5 | -6.8 |
| ULK1 | Serine/threonine-protein kinase ULK1 [Homo sapiens] | DLkPQNILLSNPAGR | Lys2 | -8.3 | -9 |
| ULK3 | Unc-51-like kinase 3 [Homo sapiens (Human)] | EVVAIKCVAk | Lys1 | -11.6 | 0.5 |
| ULK3 | Unc-51-like kinase 3 [Homo sapiens (Human)] | NISHLDLkPQNILLSLEKPHLK | Lys2 | -11.5 | 9.4 |
| Wnk1,Wnk2,Wnk3 | Serine/threonine-protein kinase WNK2 [Homo sapiens (Human)] | DLkCDNIFITGPTGSVK | Lys2 | 7.4 | -9 |
| Wnk1,Wnk2,Wnk4 | Serine/threonine-protein kinase WNK2 [Homo sapiens (Human)] | IGDLGLATLkR | Activation Loop | -5.2 | -12.8 |
| Wnk4 | Serine/threonine-protein kinase WNK4 [Homo sapiens (Human)] | DLkCDNVFITGPTGSVK | Lys2 | -16.7 | -7.1 |
| YANK3 | PKE protein kinase [Homo sapiens (Human)] | DVKPDNILLDER | Lys2 | 13.6 | -7.6 |
| YES | Proto-oncogene tyrosine-protein kinase Yes n=1 Tax=Homo sapiens RepID=YES_HUMAN | VAIKTLKPGTMMPEAFLEQAQIMK | Lys1 | -2.4 | -4.3 |
| YSK1 | Serine/threonine-protein kinase 25 [Homo sapiens (Human)] | EVVAIKIIDLEEADEIEDIQEITVLSQCDSPIYTR | Lys1 | 3.5 | 34.6 |
| ZAK | Mitogen-activated protein kinase kinase kinase MLT [Homo sapiens (Human)] | WISQDKEVAVKk | Lys1 | -3.3 | -6.3 |
| ZC1/HGK | Mitogen-activated protein kinase kinase kinase kinase 4 [Homo sapiens (Human)] | TGQLAAIKVMDVTEDEEEEIKLEINMLK | Lys1 | 17.4 | 43.7 |
| ZC1/HGK | Mitogen-activated protein kinase kinase kinase kinase 4 [Homo sapiens (Human)] | TGQLAAIKVMDVTEDEEEEIKLEINMLKK | Lys1 | 11.1 | -8.3 |
| ZC1/HGK,Z C2/TNIK,Z C3/MINK | Mitogen-activated protein kinase kinase kinase kinase 4 [Homo sapiens (Human)] | DIkGQNVLLTENAIEVK | Lys2 | -11.4 | -15.8 |
| ZC2/TNIK | TRAF2 and NCK-interacting kinase [Homo sapiens (Human)] | TGQLAAIKVMDVTGDEEEEIKQEINMLKK | Lys1 | 3.5 | -8 |

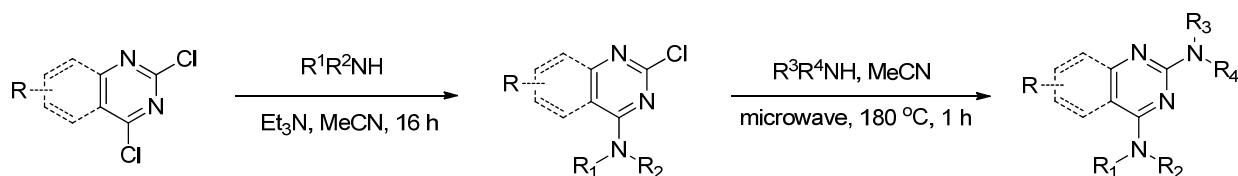
General experimental section

All reagents were used as received. Acetonitrile, DCM, toluene and THF were purified using the Innovative Technology PureSolv solvent purification system. The ^1H and ^{13}C spectra were recorded on a Bruker Avance 400 or 500 MHz spectrometer. Chemical shifts are reported in parts per million and were referenced to residual proton solvent signals. Flash column chromatography separations were performed

using the Teledyne Isco CombiFlash Rf using RediSep Rf silica gel columns. TLC was performed on Analtech UNIPLATE silica gel GHLF plates (gypsum inorganic hard layer with fluorescence). TLC plates were developed using iodine vapor. Automated preparative RP HPLC purification was performed using an Agilent 1200 Mass-Directed Fractionation system (Prep Pump G1361 with gradient extension, Make-up pump G1311A, pH modification pump G1311A, HTS PAL autosampler, UV-DAD detection G1315D, Fraction Collector G1364B, and Agilent 6120 quadrupole spectrometer G6120A). The preparative chromatography conditions included a Waters X-Bridge C18 column (19 × 150 mm, 5 μm, with 19 × 10-mm guard column), elution with a water and acetonitrile gradient, which increases 20% in acetonitrile content over 4 min at a flow rate of 20 mL/min (modified to pH 9.8 through addition of NH₄OH by auxiliary pump), and sample dilution in DMSO. The preparative gradient, triggering thresholds, and UV wavelength were selected according to the analytical RP HPLC analysis of each crude sample. The analytical method used an Agilent 1200 RRLC system with UV detection (Agilent 1200 DAD SL) and mass detection (Agilent 6224 TOF). The analytical method conditions included a Waters Aquity BEH C18 column (2.1 × 50 mm, 1.7 μm) and elution with a linear gradient of 5% acetonitrile in pH 9.8 buffered aqueous ammonium formate to 100% acetonitrile at 0.4 mL/min flow rate. Compound purity was measured on the basis of peak integration (area under the curve) from UV/vis absorbance (at 214 nm), and compound identity was determined on the basis of mass analysis.

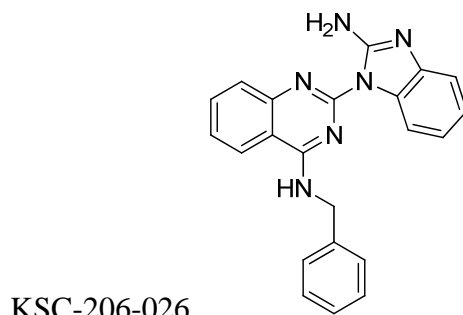
Compounds S1-S44 and S57-S69 were purchased from commercial vendors. All synthetic compounds were synthesized by one of four general synthetic methods (A to D) described below. The yield, purity and characterization of compounds synthesized by each method are compiled immediately following each method.

General Procedure A: Representative protocol for the synthesis of quinazoline analogues, synthesis and characterization for **16**, S45-S56, S70-S125, S142-S147, S156-S160, ML241, S162, S165, S169-S188.



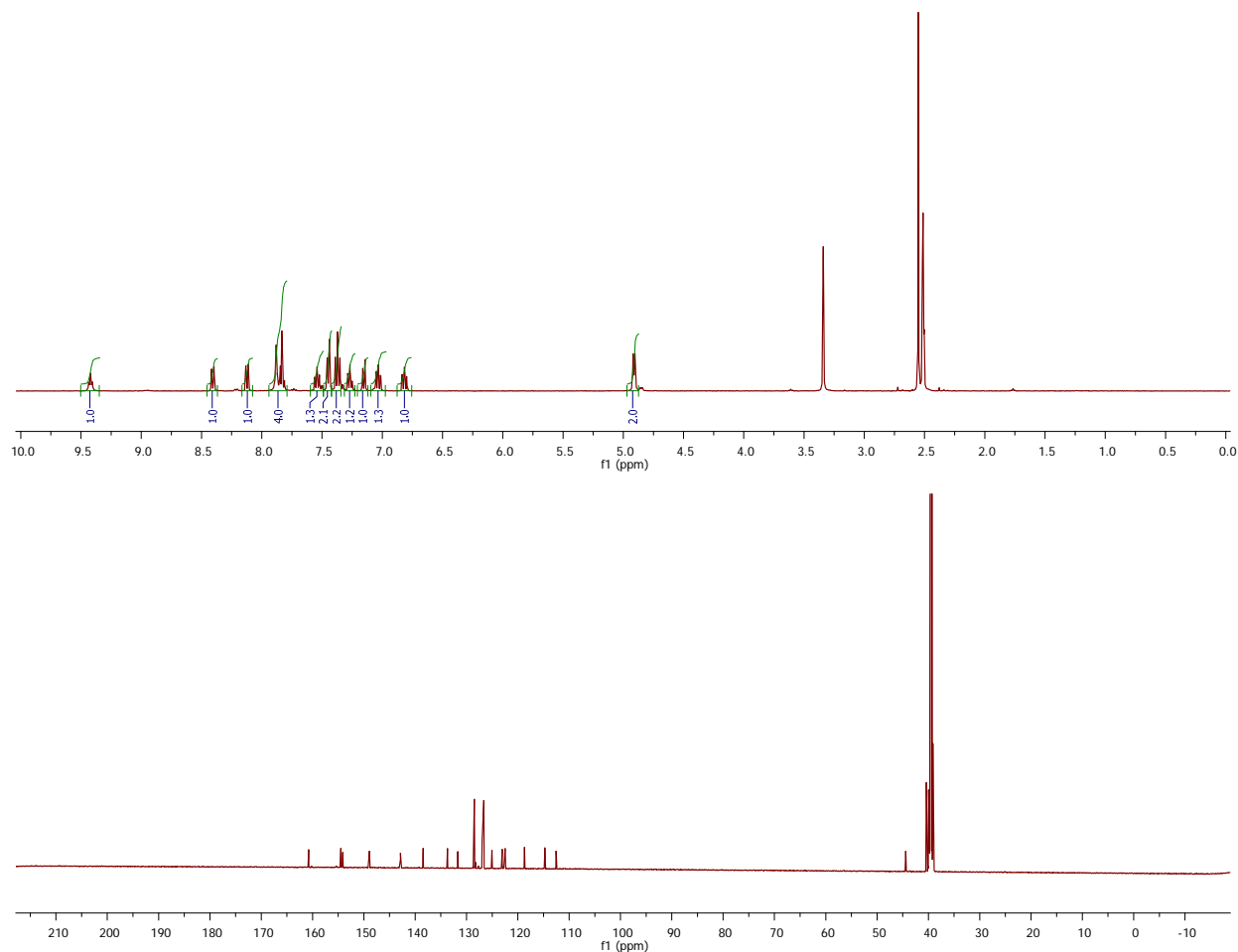
Scheme S1: General synthesis of 2,4-diaminoquinazolines

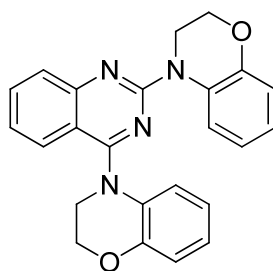
Representative procedure for the synthesis of quinazoline analogues:



***N*-Benzyl-2-chloroquinazolin-4-amine.** 2,4-dichloroquinazoline (2.4 g, 12.3 mmol) was suspended in 20 mL of THF. Triethylamine (2.1 mL, 14.7 mmol) was added, followed by the addition of benzylamine (1.4 mL, 12.9 mmol). The mixture was stirred at room temperature for 16 h. The mixture was diluted with EtOAc, filtered, and the filtrate was concentrated. The residue was purified by silica gel chromatography (EtOAc:hexanes = 1:3, R_f = 0.5) to give a colorless solid (1.6 g, 47%). ^1H NMR (400MHz, CDCl_3) δ 7.87–7.73 (m, 2H), 7.68 (d, J = 8.2 Hz, 1H), 7.54–7.32 (m, 6H), 6.10 (s, 1H), 4.90 (d, J = 5.3 Hz, 2H).

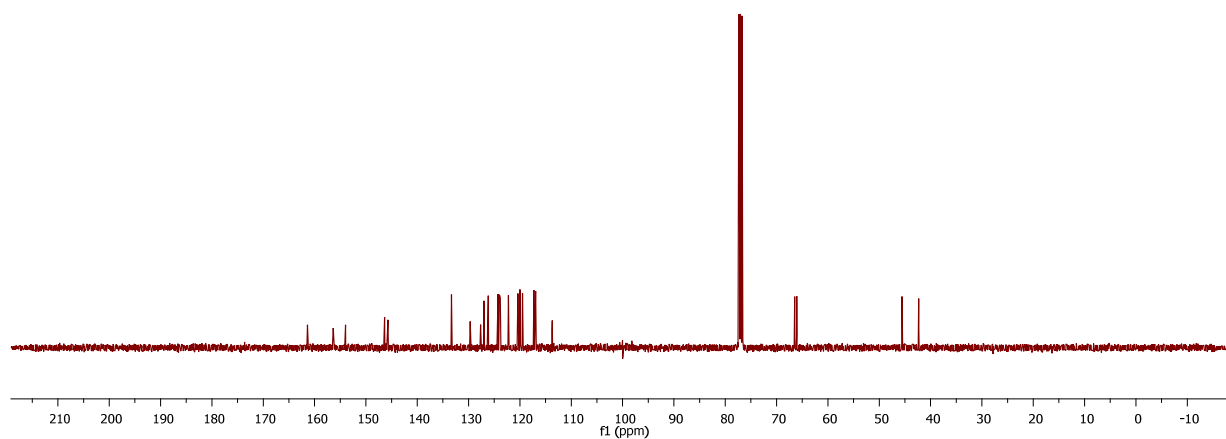
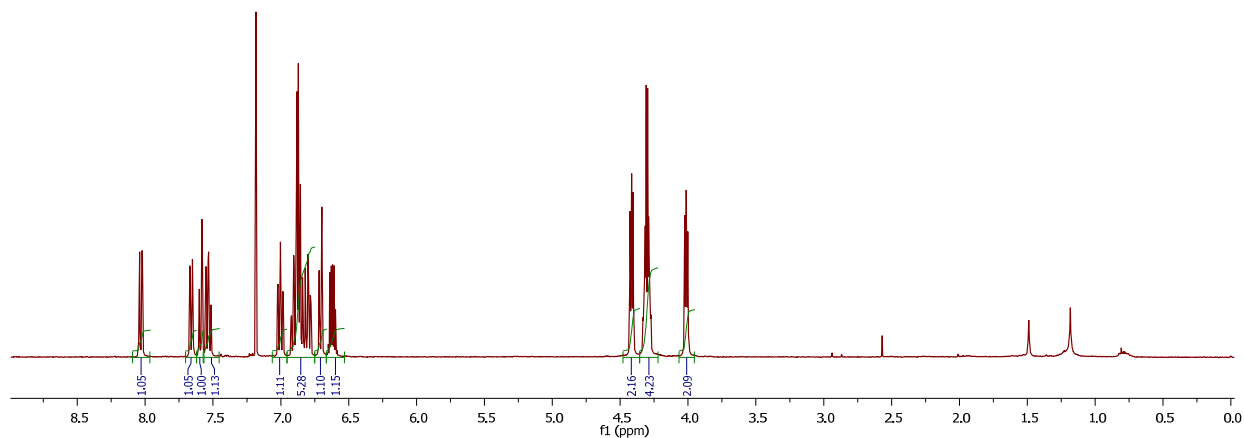
2-(2-Amino-1*H*-benzo[*d*]imidazol-1-yl)-*N*-benzylquinazolin-4-amine (16). A suspension of *N*-benzyl-2-chloroquinazolin-4-amine (0.015 g, 0.056 mmol) and 1*H*-benzo[*d*]imidazol-2-amine (0.015 g, 0.111 mmol) in Acetonitrile (1 ml) was heated in microwave at 180 °C for 1 h. Solvent was removed and the crude sample was purified via reverse phase preparative HPLC. Yield: 6.8 mg, 33%. ^1H NMR (400 MHz, DMSO) δ 9.42 (t, J = 5.8 Hz, 1H), 8.41 (d, J = 8.1 Hz, 1H), 8.12 (d, J = 7.5 Hz, 1H), 7.94 – 7.79 (m, 4H), 7.54 – 7.50 (m, 1H), 7.45 (d, J = 7.1 Hz, 2H), 7.37 (t, J = 7.6 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 7.1 Hz, 1H), 7.03 (td, J = 1.2, 7.6 Hz, 1H), 6.88 – 6.76 (m, 1H), 4.91 (d, J = 5.8 Hz, 2H). ^{13}C NMR (126 MHz, DMSO) δ 160.7, 154.5, 154.1, 148.9, 142.8, 138.4, 133.7, 131.7, 128.5, 127.0, 126.6, 125.1, 123.0, 122.5, 118.7, 114.8, 112.5, 44.4. HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{19}\text{N}_6$ ($M+H$) 367.1671; found 367.1685.

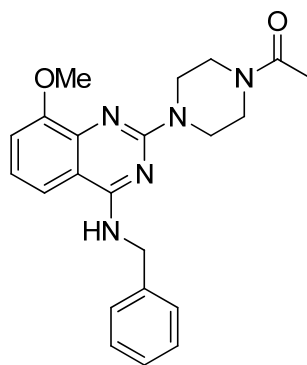




KSC-16-190

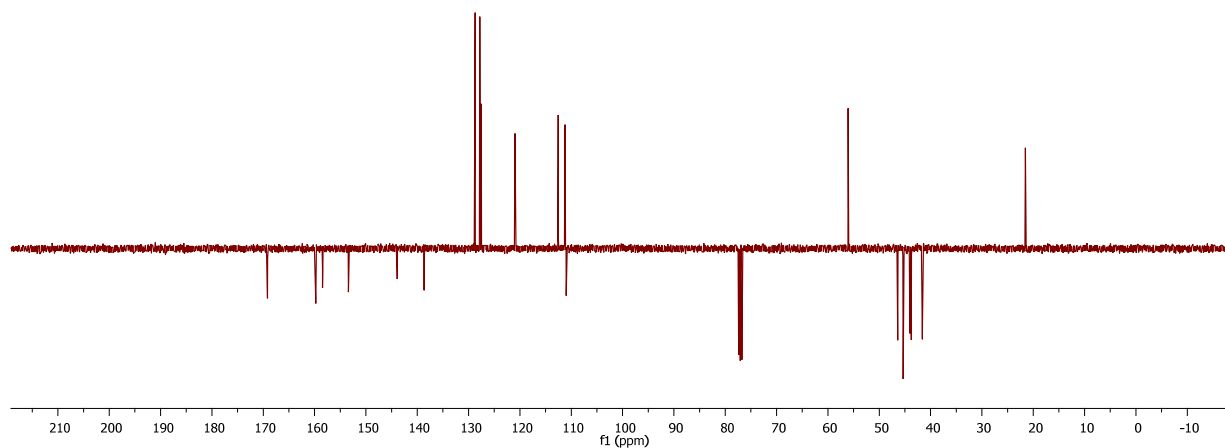
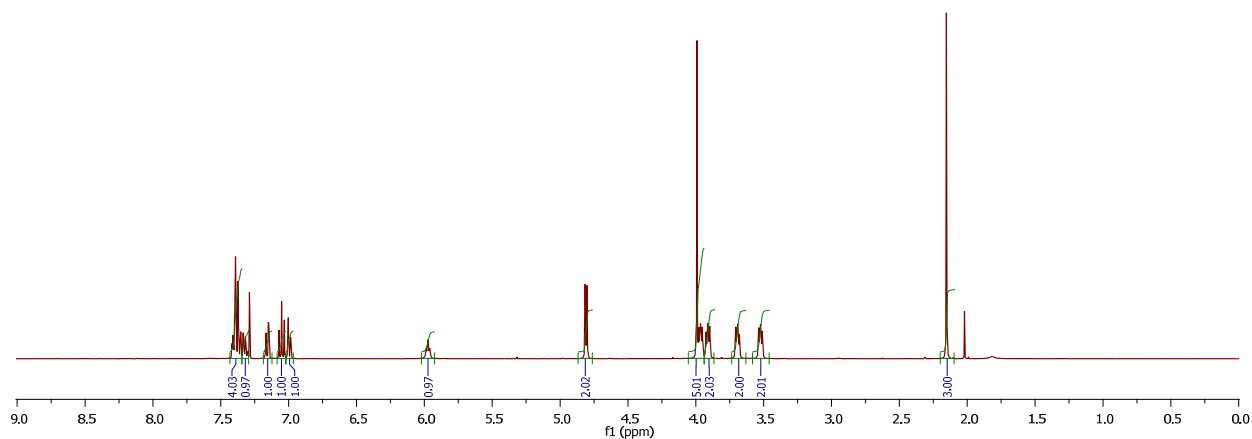
4,4'-(Quinazoline-2,4-diyl)bis(3,4-dihydro-2H-benzo[b][1,4]oxazine) (S45). Yield: 10.4 mg, 33%. ^1H NMR (400 MHz, CDCl_3) δ 8.03 (dd, $J = 1.5, 8.2$ Hz, 1H), 7.66 (dd, $J = 0.8, 8.4$ Hz, 1H), 7.59 (dd, $J = 0.8, 8.5$ Hz, 1H), 7.53 (ddd, $J = 1.4, 6.7, 8.4$ Hz, 1H), 7.00 (ddd, $J = 1.4, 6.7, 8.2$ Hz, 1H), 6.96 – 6.75 (m, 5H), 6.71 (d, $J = 8.1$ Hz, 1H), 6.67 – 6.53 (m, 1H), 4.48 – 4.36 (m, 2H), 4.36 – 4.22 (m, 4H), 4.07 – 3.95 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 161.4, 156.4, 154.0, 146.4, 145.7, 133.3, 129.7, 127.7, 127.0, 126.2, 124.3, 124.0, 123.8, 122.2, 120.4, 120.0, 119.5, 117.3, 117.0, 113.7, 66.5, 66.1, 45.6, 42.3. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{21}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) 397.1665; found 397.1664.

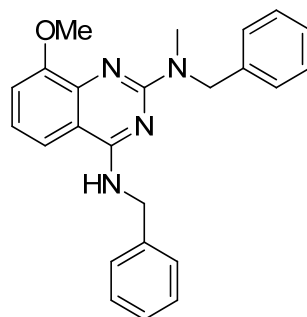




KSC-16-272

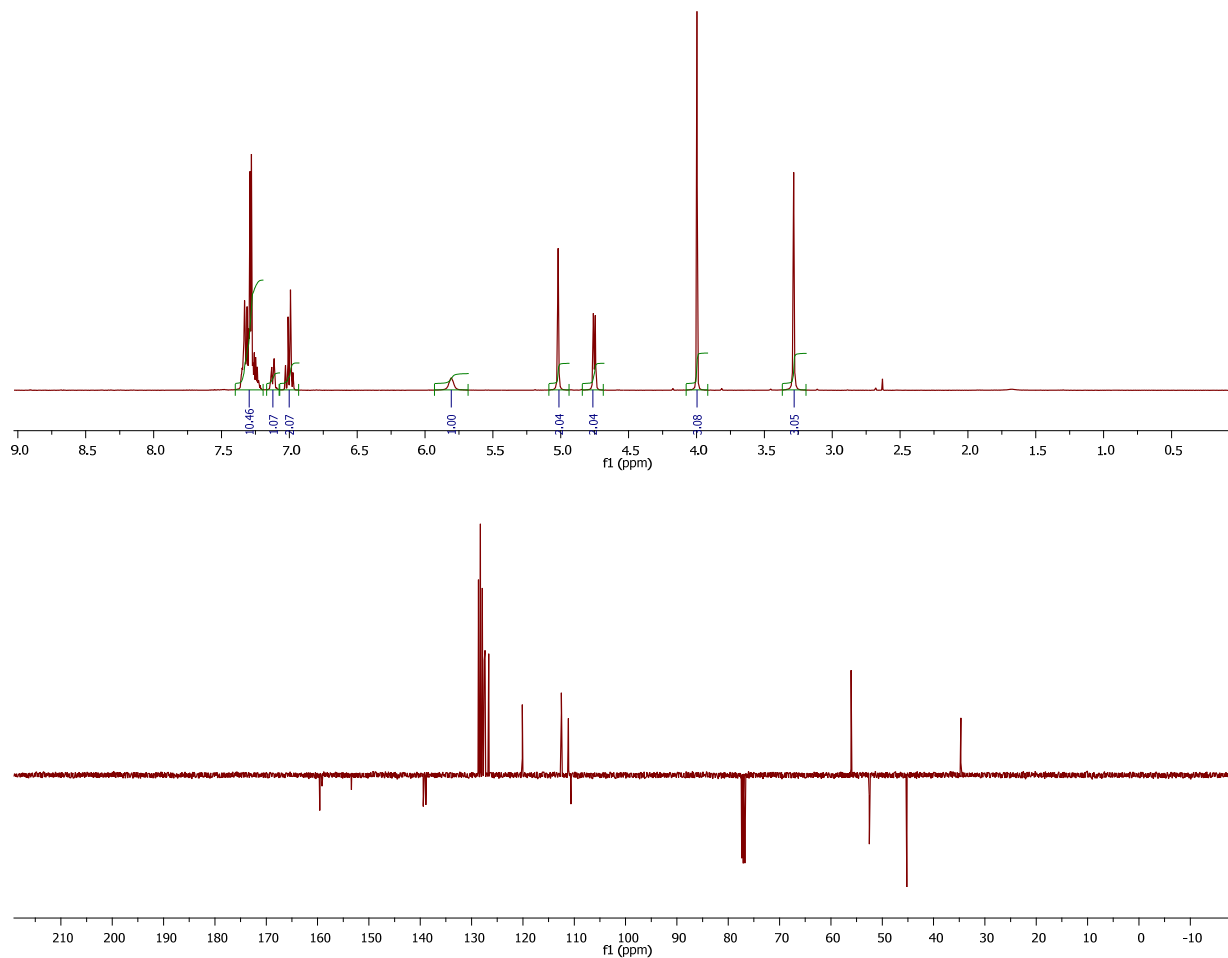
1-(4-(4-(benzylamino)-8-methoxyquinazolin-2-yl)piperazin-1-yl)ethanone (S46). Yield: 20.6 mg, 79%. ^1H NMR (400 MHz, CDCl_3) δ 7.43 – 7.34 (m, 4H), 7.34 – 7.29 (m, 1H), 7.16 (dd, J = 1.3, 8.2 Hz, 1H), 7.05 (t, J = 7.9 Hz, 1H), 6.99 (dd, J = 1.2, 7.8 Hz, 1H), 5.97 (t, J = 5.3 Hz, 1H), 4.81 (d, J = 5.4 Hz, 2H), 3.99 (s, 3H), 3.98 – 3.94 (m, 2H), 3.91 (dd, J = 4.3, 6.3 Hz, 2H), 3.74 – 3.63 (m, 2H), 3.58 – 3.46 (m, 2H), 2.15 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 169.2, 159.8, 158.4, 153.4, 143.9, 138.7, 128.7, 127.8, 127.5, 121.0, 112.6, 111.2, 111.0, 56.1, 46.4, 45.4, 44.0, 43.8, 41.6, 21.5. HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{26}\text{N}_5\text{O}_2$ ($\text{M}+\text{H}$) 392.2087; found 392.2084.

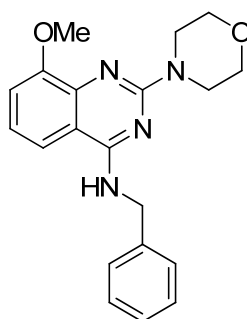




KSC-16-277

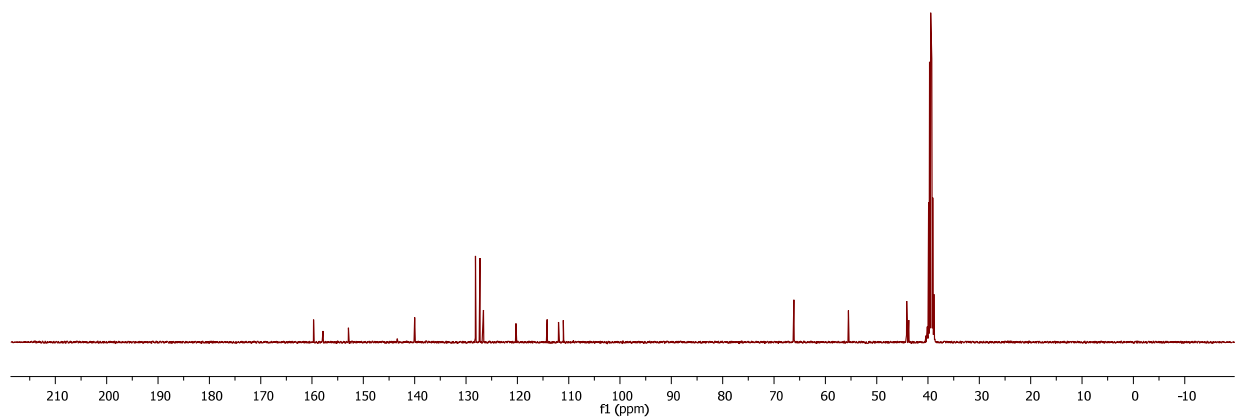
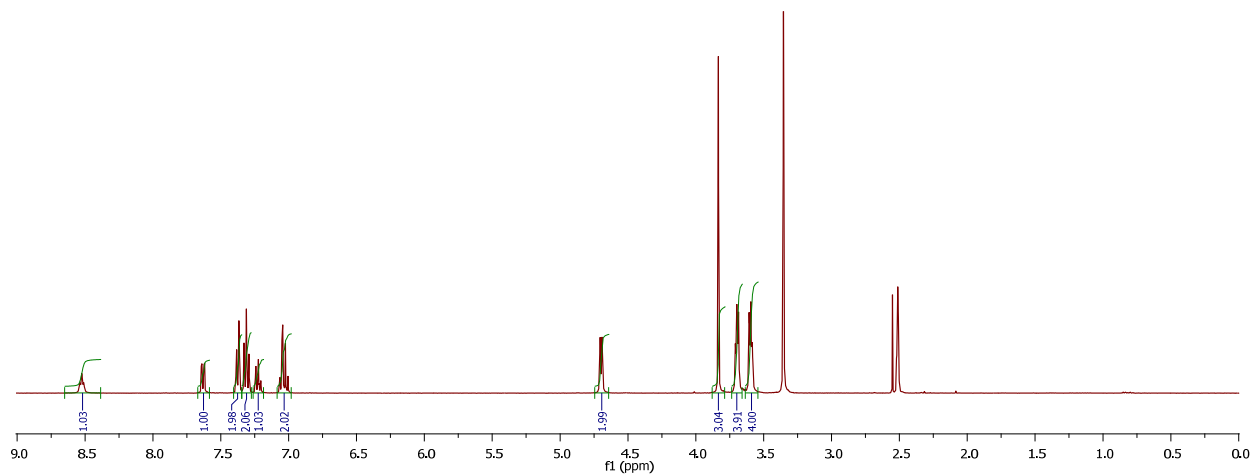
***N*²,*N*⁴-Dibenzyl-8-methoxy-*N*²-methylquinazoline-2,4-diamine (S47).** Yield: 21.8 mg, 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.40 – 7.19 (m, 10H), 7.12 (dd, *J* = 2.0, 7.3 Hz, 1H), 7.07 – 6.93 (m, 2H), 5.81 (s, 1H), 5.02 (s, 2H), 4.75 (d, *J* = 5.5 Hz, 2H), 4.00 (s, 3H), 3.28 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.6, 159.1, 153.4, 139.4, 138.9, 128.7, 128.3, 127.9, 127.5, 127.4, 126.7, 120.1, 112.5, 111.1, 110.6, 56.1, 52.5, 45.2, 34.7. HRMS (*m/z*): calcd for C₂₄H₂₅N₄O (*M*+*H*) 385.2028; found 385.2024.

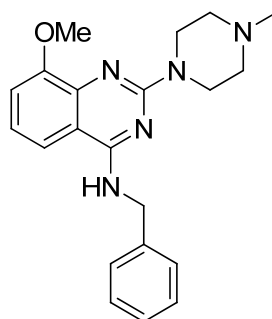




KSC-25-10

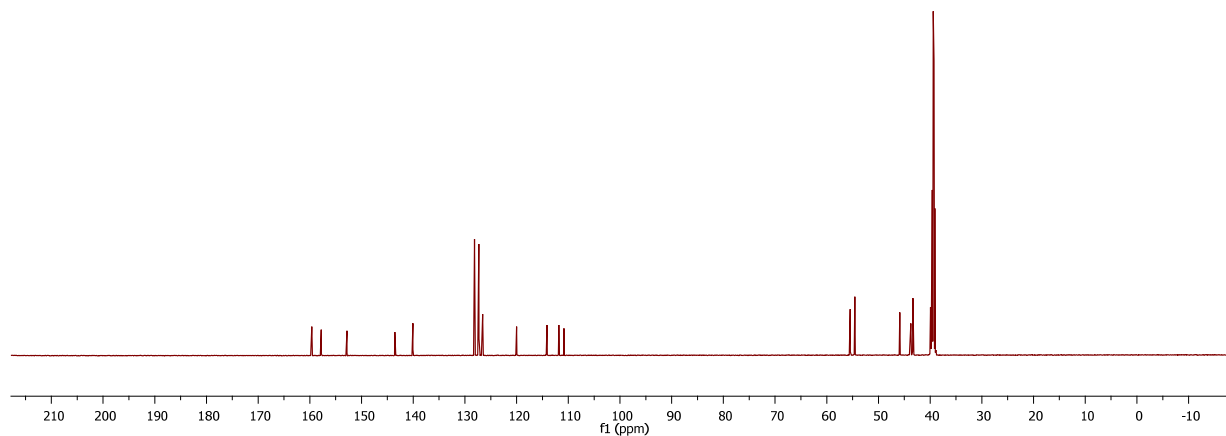
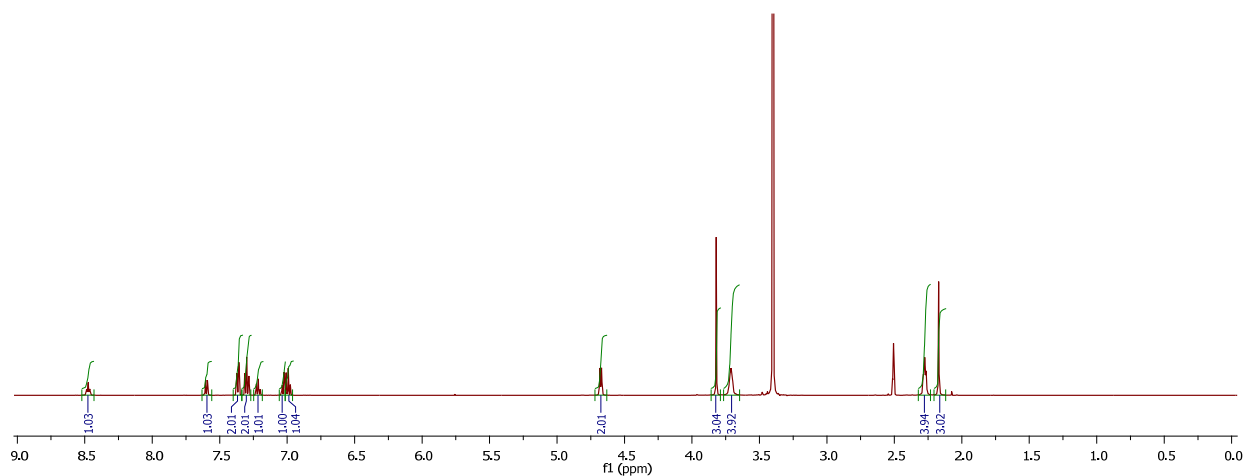
***N*-Benzyl-8-methoxy-2-morpholinoquinazolin-4-amine (S48).** Yield: 14.2 mg, 81%. ^1H NMR (400 MHz, DMSO) δ 8.52 (t, $J = 5.7$ Hz, 1H), 7.63 (dd, $J = 1.9, 7.6$ Hz, 1H), 7.41 – 7.35 (m, 2H), 7.35 – 7.28 (m, 2H), 7.26 – 7.18 (m, 1H), 7.08 – 6.98 (m, 2H), 4.70 (d, $J = 5.8$ Hz, 2H), 3.83 (s, 3H), 3.74 – 3.66 (m, 4H), 3.64 – 3.54 (m, 4H). ^{13}C NMR (101 MHz, DMSO) δ 159.7, 157.9, 152.9, 143.4, 140.0, 128.2, 127.3, 126.6, 120.3, 114.2, 112.0, 111.0, 66.1, 55.5, 44.2, 43.7. HRMS (m/z): calcd for $\text{C}_{20}\text{H}_{23}\text{N}_4\text{O}_2$ ($M+H$) 351.1821; found 351.1814.

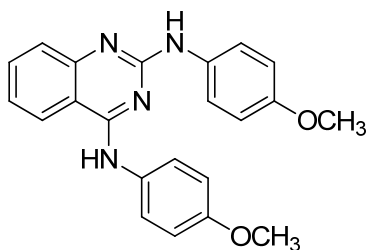




KSC-25-16

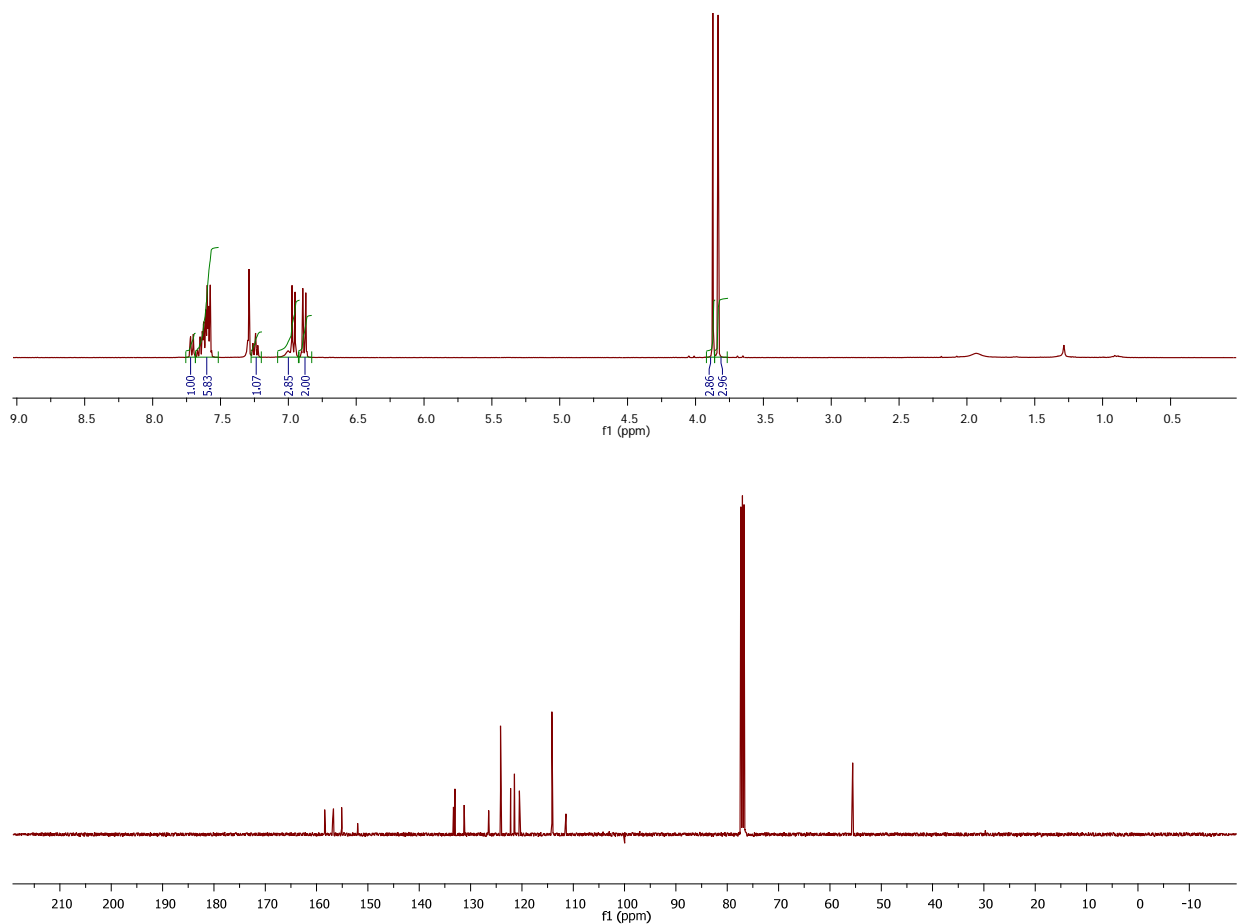
***N*-Benzyl-8-methoxy-2-(4-methylpiperazin-1-yl)quinazolin-4-amine (S49).** Yield: 12.0 mg, 66%. ^1H NMR (500 MHz, DMSO) δ 8.47 (t, $J = 5.9$ Hz, 1H), 7.60 (dd, $J = 1.4, 8.0$ Hz, 1H), 7.37 (d, $J = 7.1$ Hz, 2H), 7.30 (dd, $J = 4.8, 10.3$ Hz, 2H), 7.21 (t, $J = 7.3$ Hz, 1H), 7.03 (dd, $J = 1.3, 7.8$ Hz, 1H), 6.99 (t, $J = 7.8$ Hz, 1H), 4.68 (d, $J = 5.8$ Hz, 2H), 3.82 (s, 3H), 3.71 (s, 4H), 2.27 (t, $J = 4.9$ Hz, 4H), 2.17 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 159.6, 157.8, 152.8, 143.6, 140.1, 128.1, 127.3, 126.6, 120.0, 114.1, 111.8, 110.8, 55.5, 54.6, 45.9, 43.7, 43.3. HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{26}\text{N}_5\text{O}$ ($M+H$) 364.2137; found 364.2142.

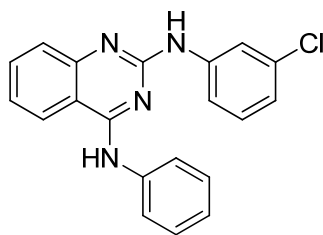




KSC-16-149

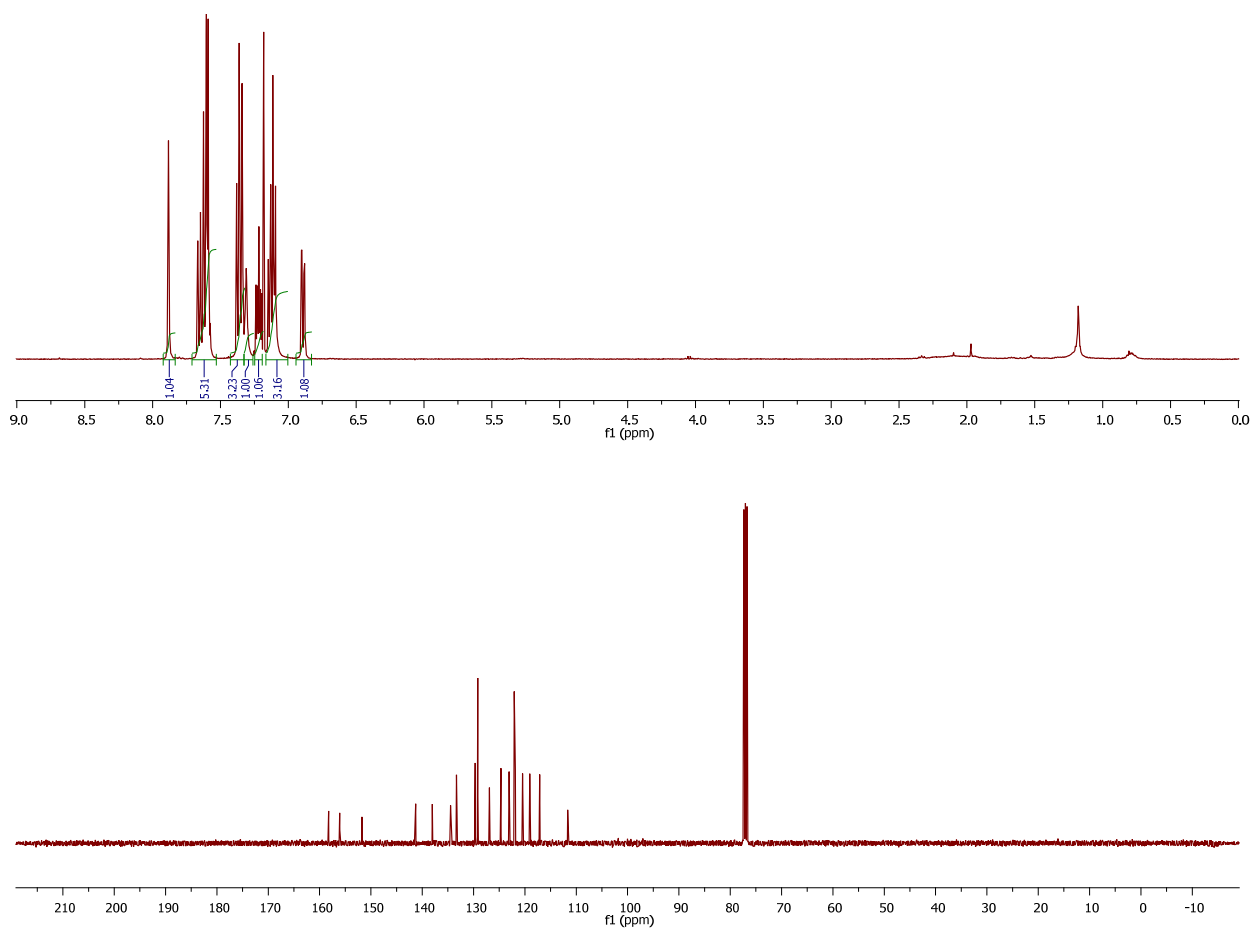
***N*²,*N*⁴-Bis(4-methoxyphenyl)quinazoline-2,4-diamine (S50).** Yield: 11.9 mg, 91%. ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.52 (m, 6H), 7.29 (s, br. 1H), 7.24 (ddd, *J* = 1.7, 6.5, 8.2 Hz, 1H), 7.08 – 6.92 (m, 3H), 6.93 – 6.83 (m, 2H), 3.87 (s, 3H), 3.83 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.4, 156.9, 156.7, 155.1, 152.0, 133.3, 133.0, 131.3, 126.5, 124.2, 122.2, 121.5, 120.5, 114.2, 114.0, 111.4, 55.58, 55.56. HRMS (*m/z*): calcd for C₂₂H₂₁N₄O₂ (*M*+H) 373.1665; found 373.1659.

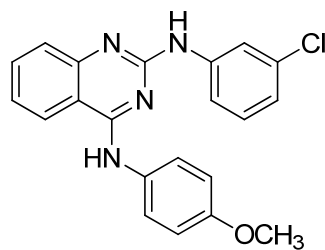




KSC-16-163

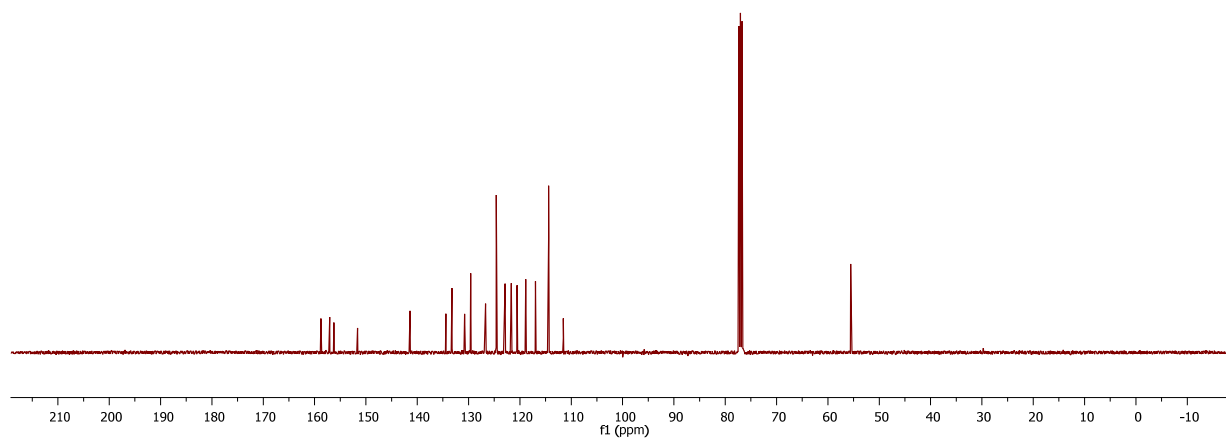
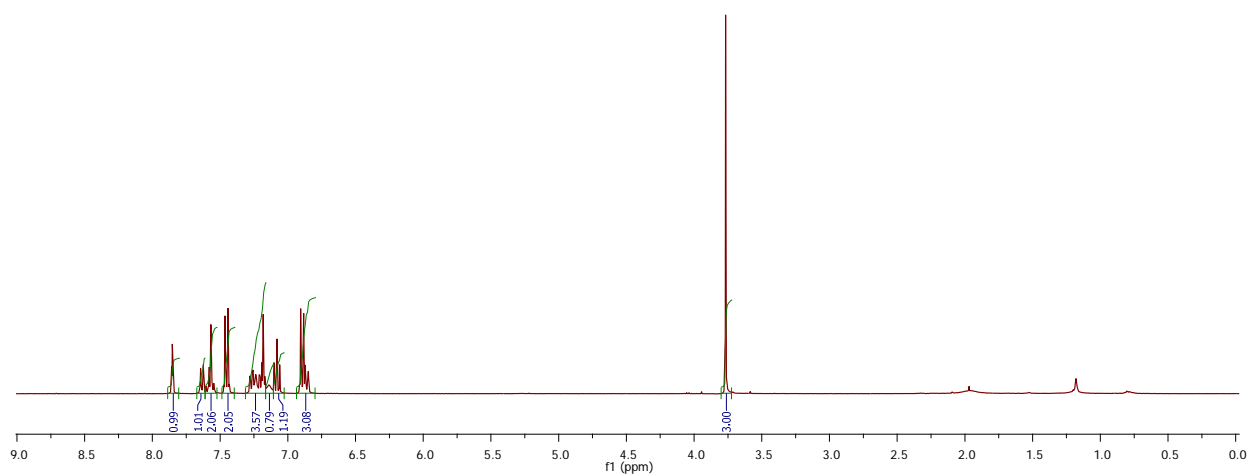
***N*²-(3-Chlorophenyl)-*N*⁴-phenylquinazoline-2,4-diamine (S51).** Yield: 13.0 mg, 96%. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (t, *J* = 2.0 Hz, 1H), 7.71 – 7.53 (m, 5H), 7.37 (dd, *J* = 5.2, 10.7 Hz, 3H), 7.31 (s, br. 1H), 7.22 (ddd, *J* = 2.9, 5.3, 8.2 Hz, 1H), 7.17 – 7.00 (m, 3H), 6.89 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 158.2, 156.1, 151.8, 141.3, 138.1, 134.5, 133.3, 129.7, 129.2, 126.9, 124.7, 123.1, 122.1, 121.9, 120.5, 119.1, 117.1, 111.7. HRMS (*m/z*): calcd for C₂₀H₁₆ClN₄ (M+H) 347.1063; found 347.1061.

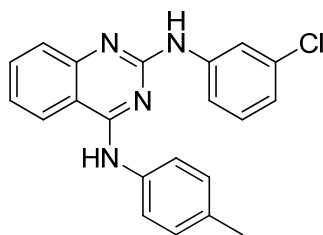




KSC-16-164

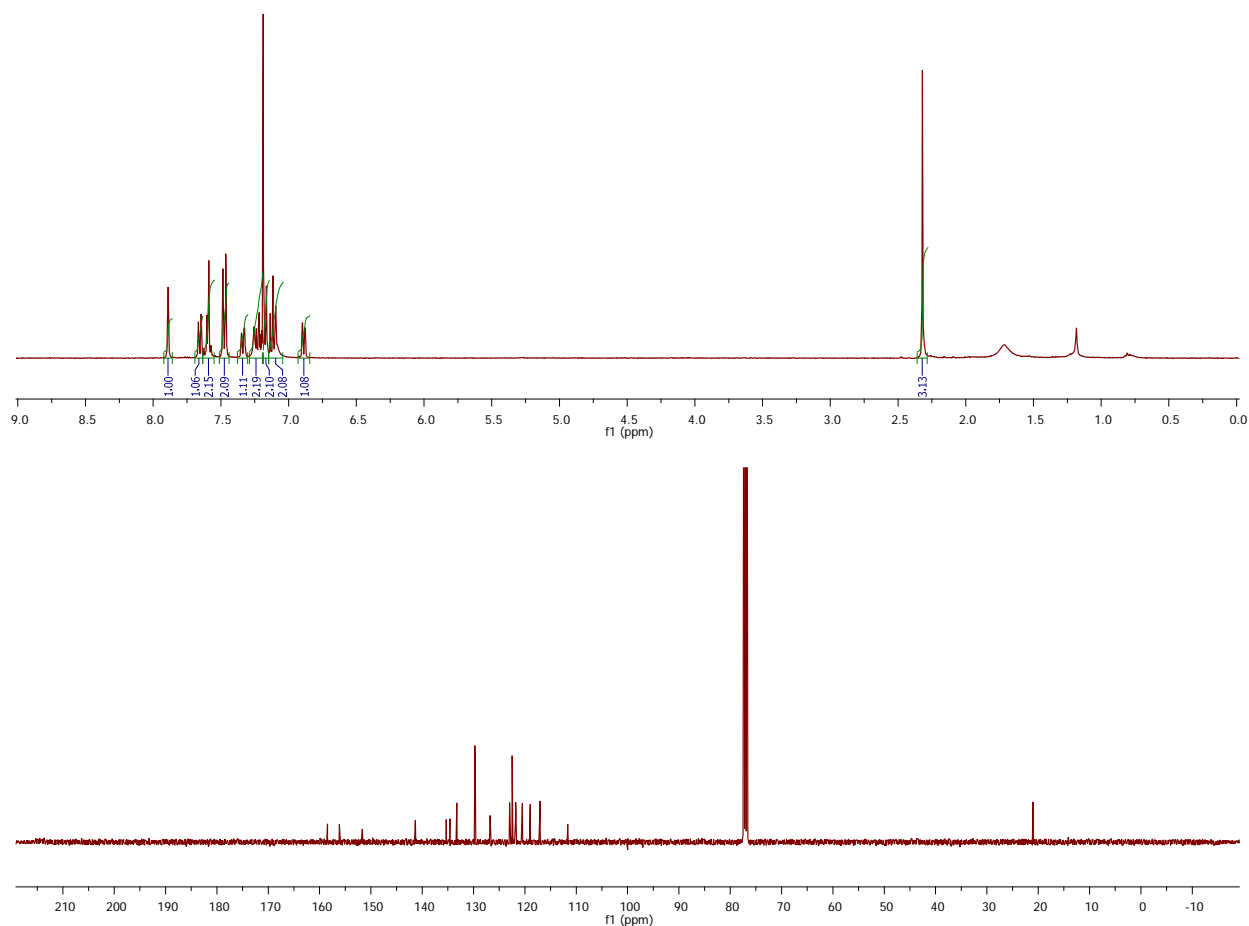
***N*²-(3-Chlorophenyl)-*N*⁴-(4-methoxyphenyl)quinazoline-2,4-diamine (S52).** Yield: 13.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.85 (t, *J* = 2.0 Hz, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.61 – 7.52 (m, 2H), 7.49 – 7.39 (m, 2H), 7.31 – 7.11 (m, 4H), 7.08 (t, *J* = 8.1 Hz, 1H), 6.94 – 6.80 (m, 3H), 3.77 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.8, 157.1, 156.2, 151.6, 141.4, 134.4, 133.3, 130.8, 129.6, 126.7, 124.6, 122.9, 121.7, 120.6, 118.9, 117.0, 114.4, 111.6, 55.6. HRMS (*m/z*): calcd for C₂₁H₁₈ClN₄O (*M*+*H*) 377.1169; found 377.1169.

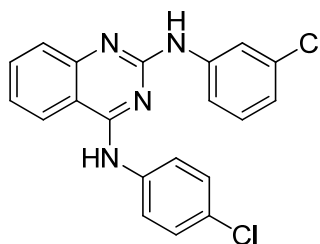




KSC-16-174

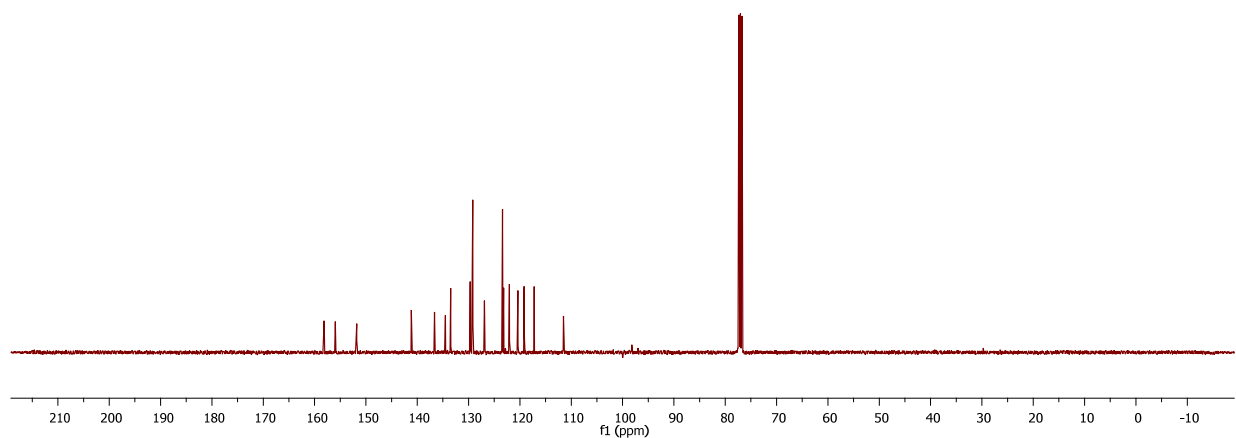
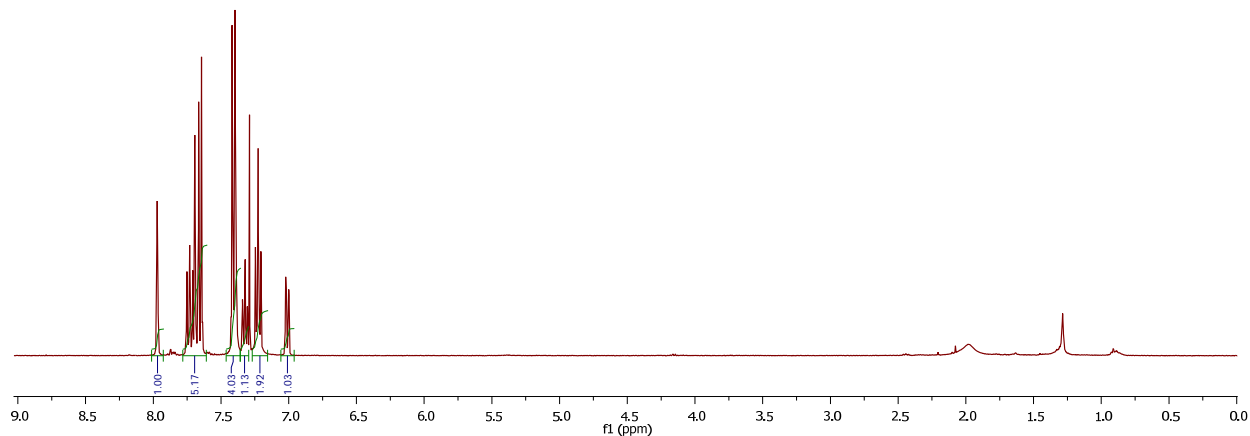
***N*²-(3-Chlorophenyl)-*N*⁴-(*p*-tolyl)quinazoline-2,4-diamine (S53).** Yield: 5.7 mg, 69%. ¹H NMR (400 MHz, CDCl₃) δ 7.89 (t, *J* = 2.0 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.60 (dd, *J* = 1.6, 5.1 Hz, 2H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.30 (m, 1H), 7.22 (ddd, *J* = 4.7, 7.4, 8.2 Hz, 2H), 7.16 (s, br. 2H), 7.12 (t, *J* = 8.1 Hz, 2H), 6.89 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H), 2.32 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.5, 156.1, 151.7, 141.4, 135.3, 134.6, 134.5, 133.3, 129.7, 129.6, 126.8, 123.0, 122.5, 121.8, 120.5, 119.0, 117.0, 111.7, 21.0. HRMS (*m/z*): calcd for C₂₁H₁₈ClN₄ (*M*+*H*) 361.1220; found 361.1228.

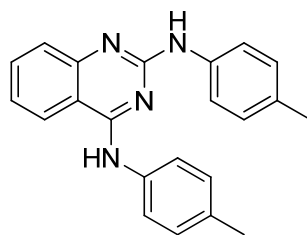




KSC-16-176

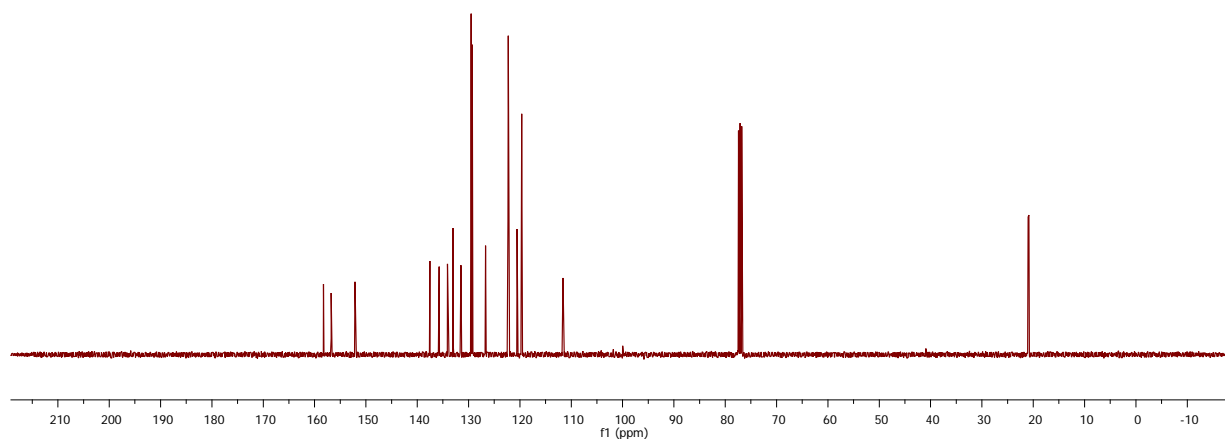
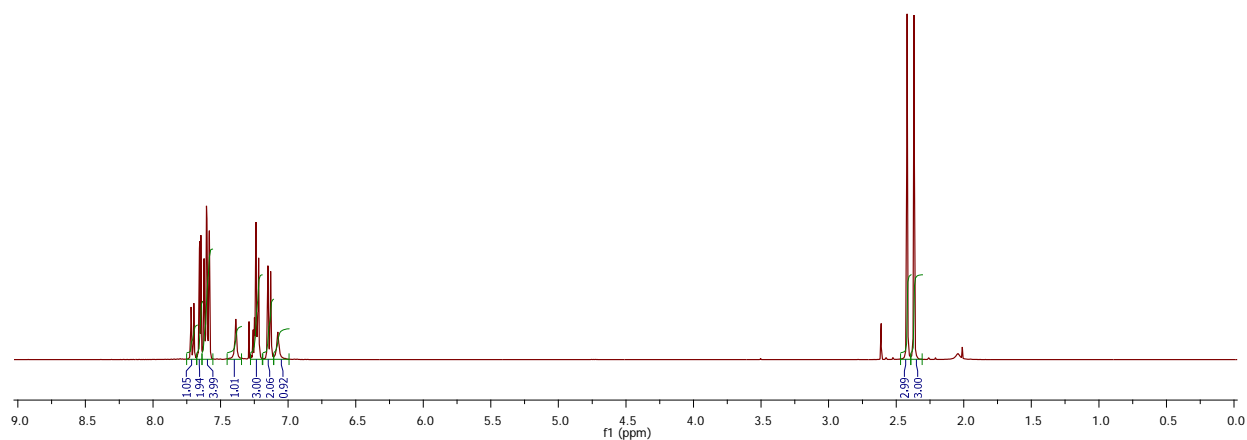
***N*²-(3-Chlorophenyl)-*N*⁴-(4-chlorophenyl)quinazoline-2,4-diamine (S54).** Yield: 13.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.97 (t, *J* = 2.0 Hz, 1H), 7.78 – 7.61 (m, 5H), 7.46 – 7.36 (m, 4H), 7.32 (ddd, *J* = 2.1, 6.1, 8.2 Hz, 1H), 7.23 (t, *J* = 8.0 Hz, 2H), 7.01 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 158.1, 156.0, 151.8, 141.2, 136.6, 134.5, 133.5, 129.7, 129.7, 129.2, 126.9, 123.4, 123.2, 122.1, 120.4, 119.2, 117.2, 111.5. HRMS (*m/z*): calcd for C₂₀H₁₅Cl₂N₄ (*M*+*H*) 381.0674; found 381.0668.

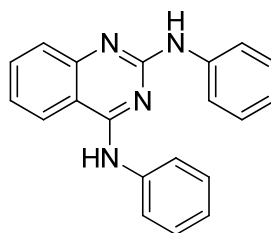




KSC-16-151

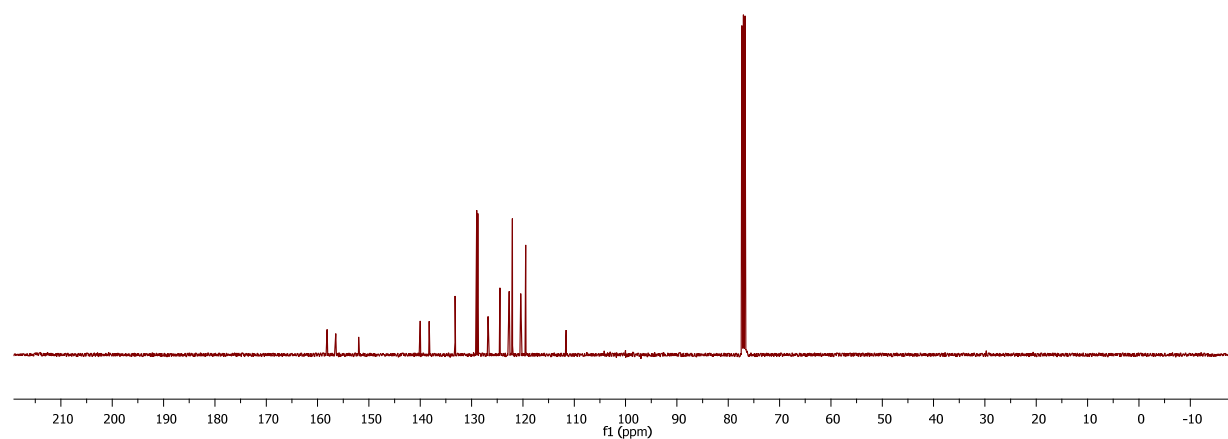
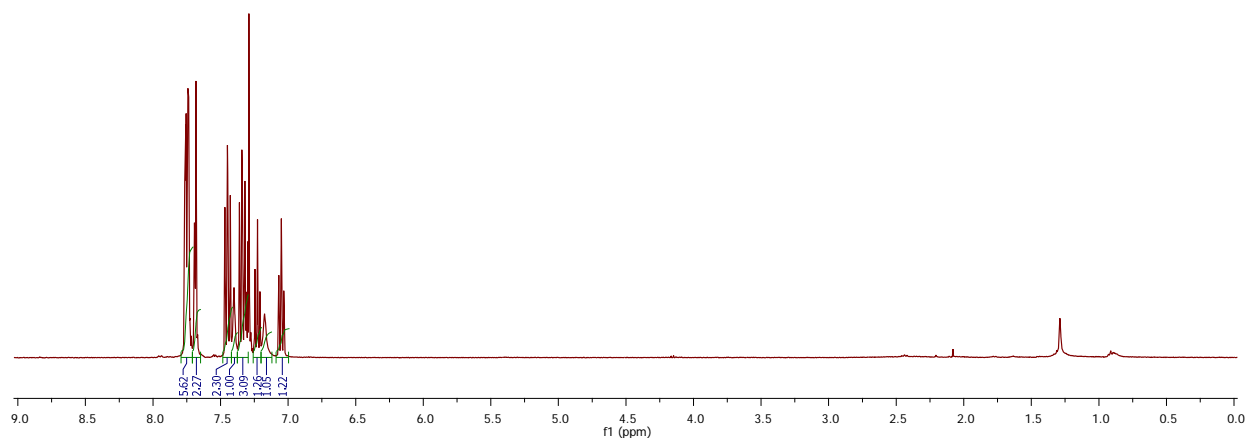
***N*²,*N*⁴-Di-*p*-tolylquinazoline-2,4-diamine (S55).** Yield: 37.8 mg, 44%. ¹H NMR (400 MHz, CDCl₃) δ 7.70 (t, *J* = 8.0 Hz, 1H), 7.66 (dd, *J* = 3.8, 4.5 Hz, 2H), 7.64 – 7.56 (m, 4H), 7.39 (s, br. 1H), 7.28 – 7.19 (m, 3H), 7.14 (d, *J* = 8.1 Hz, 2H), 7.08 (s, br. 1H), 2.42 (s, 3H), 2.37 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 158.3, 156.8, 152.1, 137.6, 135.7, 134.1, 133.0, 131.5, 129.5, 129.3, 126.7, 122.3, 122.3, 120.6, 119.7, 111.6, 21.0, 20.9. HRMS (*m/z*): calcd for C₂₂H₂₁N₄ (*M*+*H*) 341.1766; found 341.1759.

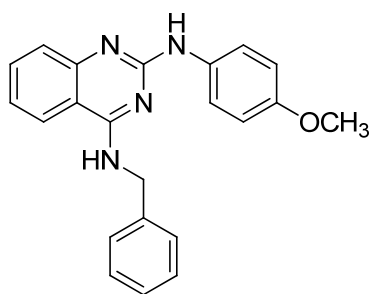




KSC-16-146

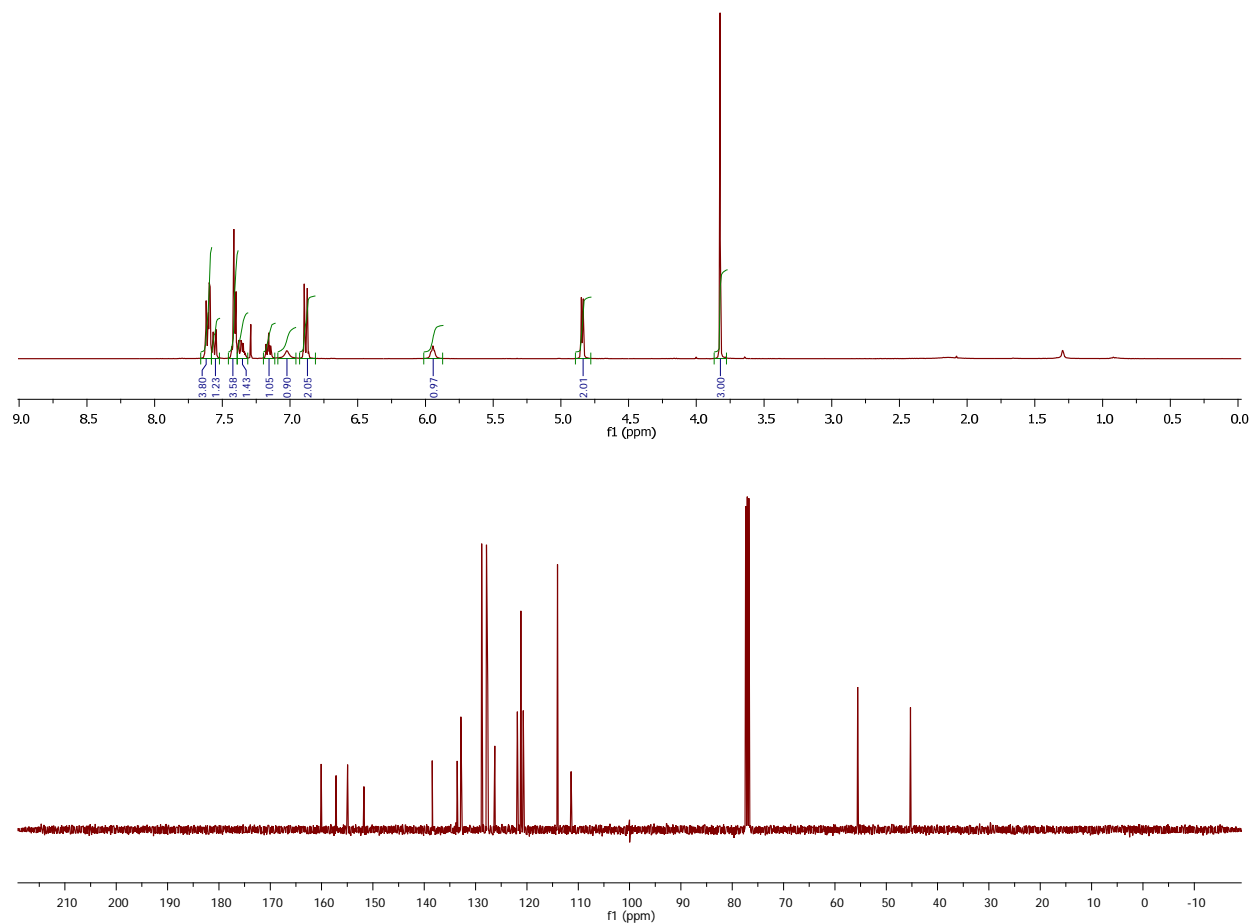
***N*²,*N*⁴-Diphenylquinazoline-2,4-diamine (S56).** Yield: 11.8 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.79 – 7.71 (m, 6H), 7.71 – 7.65 (m, 2H), 7.48 – 7.42 (m, 2H), 7.40 (s, br. 1H), 7.38 – 7.29 (m, 3H), 7.26 – 7.20 (m, 1H), 7.17 (s, br. 1H), 7.09 – 7.00 (m, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 158.2, 156.5, 152.0, 140.0, 138.3, 133.2, 129.0, 128.8, 126.8, 124.5, 122.7, 122.1, 122.1, 120.4, 119.5, 111.6. HRMS (m/z): calcd for C₂₀H₁₇N₄ (M+H) 313.1453; found 313.1451.

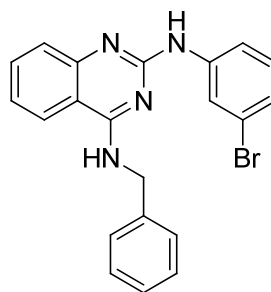




KSC-1-290

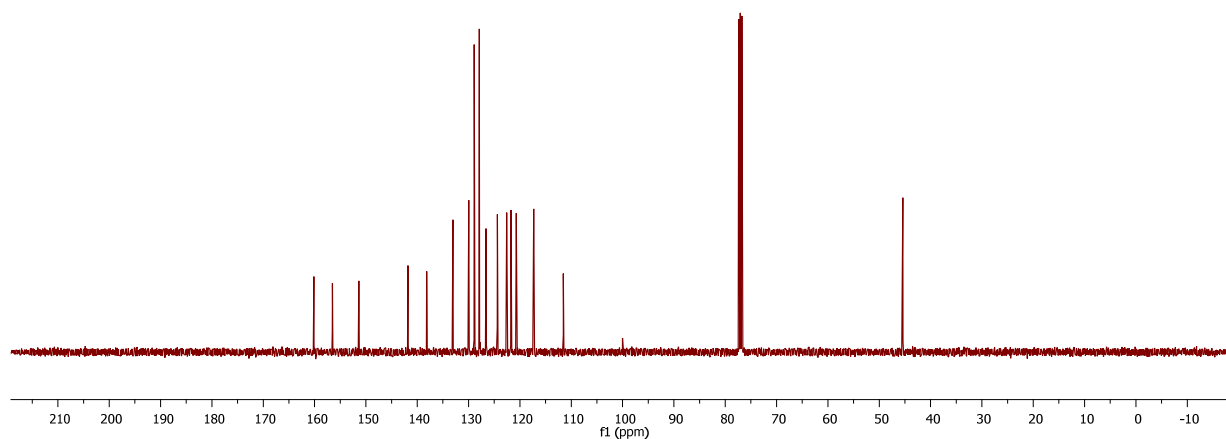
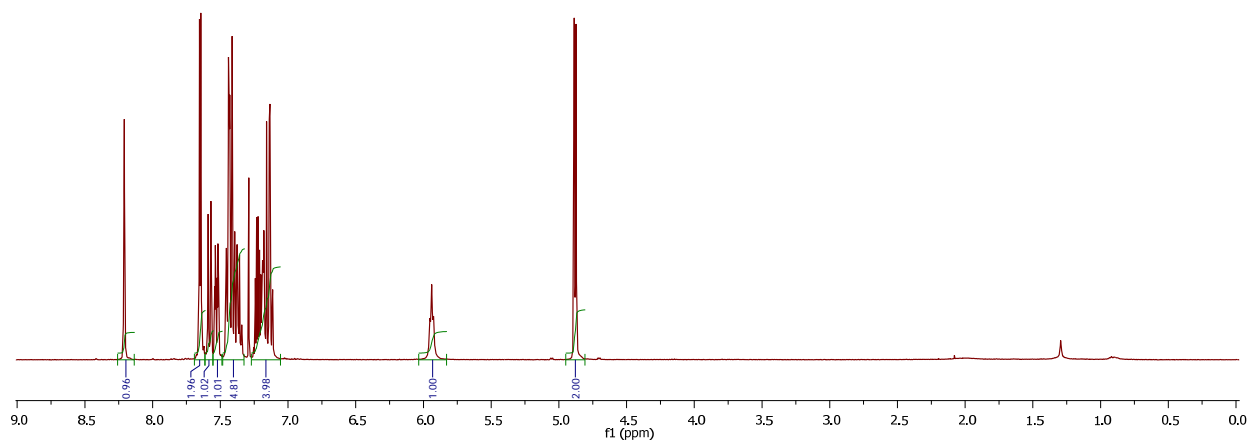
***N*⁴-Benzyl-*N*²-(4-methoxyphenyl)quinazoline-2,4-diamine (S70).** Yield: 32.0 mg, 48%. ¹H NMR (400 MHz, CDCl₃) δ 7.66 – 7.58 (m, 4H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.46 – 7.39 (m, 4H), 7.37 – 7.33 (m, 1H), 7.16 (ddd, *J* = 2.3, 5.8, 8.2 Hz, 1H), 7.02 (s, br. 1H), 6.93 – 6.81 (m, 2H), 5.95 (s, br. 1H), 4.84 (d, *J* = 5.3 Hz, 2H), 3.82 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 157.2, 154.9, 151.8, 138.4, 133.6, 132.9, 128.8, 127.9, 127.6, 126.3, 121.9, 121.2, 120.7, 114.0, 111.4, 55.6, 45.3. HRMS (*m/z*): calcd for C₂₂H₂₁N₄O (*M*+H) 357.1715; found 357.1711.

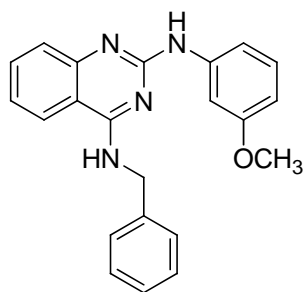




KSC-1-293

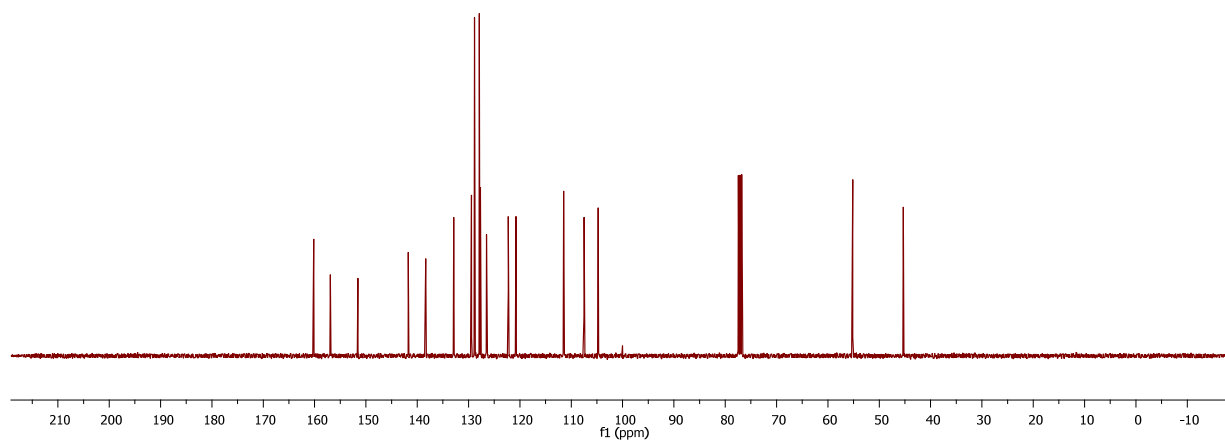
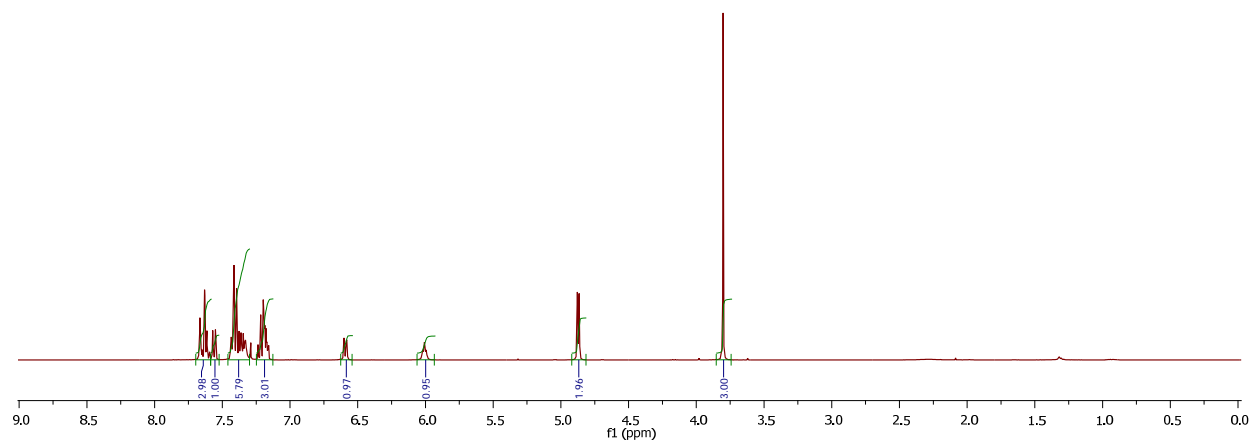
***N*⁴-Benzyl-*N*²-(3-bromophenyl)quinazoline-2,4-diamine (S71).** Yield: 47.0 mg, 63%. ¹H NMR (400 MHz, CDCl₃) δ 8.21 (t, *J* = 1.9 Hz, 1H), 7.64 (t, *J* = 6.5 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.55 – 7.49 (m, 1H), 7.48 – 7.33 (m, 5H), 7.27 – 7.06 (m, 4H), 5.93 (t, *J* = 5.4 Hz, 1H), 4.88 (d, *J* = 5.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.4, 141.8, 138.2, 133.0, 130.0, 128.9, 127.9, 127.8, 126.6, 124.4, 122.6, 122.6, 121.7, 120.7, 117.3, 111.6, 45.4. HRMS (*m/z*): calcd for C₂₁H₁₈BrN₄ (M+H) 405.0715 and 407.0694; found 407.0691.

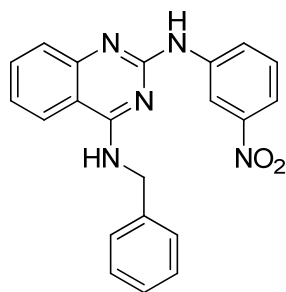




KSC-1-291

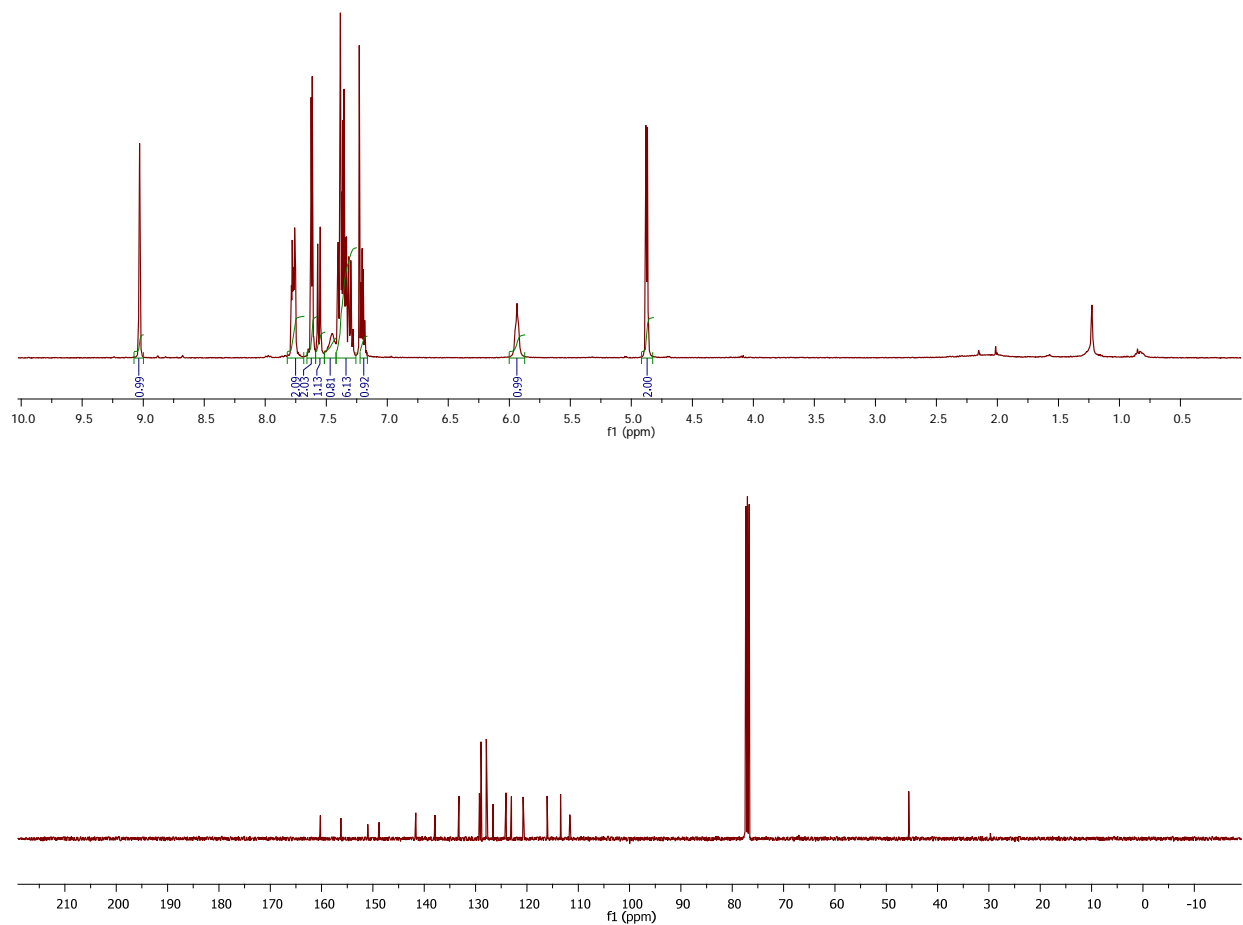
***N*⁴-Benzyl-*N*²-(3-methoxyphenyl)quinazoline-2,4-diamine (S72).** Yield: 64.0 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.70 – 7.59 (m, 3H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.46 – 7.30 (m, 6H), 7.25 – 7.13 (m, 3H), 6.59 (ddd, *J* = 1.6, 2.4, 7.6 Hz, 1H), 6.01 (t, *J* = 5.3 Hz, 1H), 4.87 (d, *J* = 5.4 Hz, 2H), 3.81 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 160.2, 156.9, 151.6, 141.7, 138.4, 132.9, 129.4, 128.9, 127.9, 127.7, 126.5, 122.3, 120.8, 111.50, 111.47, 107.5, 104.7, 55.2, 45.3. HRMS (*m/z*): calcd for C₂₂H₂₁N₄O (*M*+*H*) 357.1715; found 357.1715.

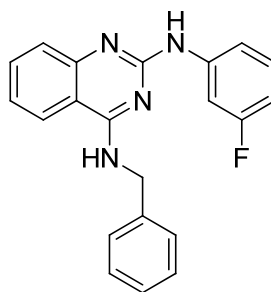




KSC-16-155

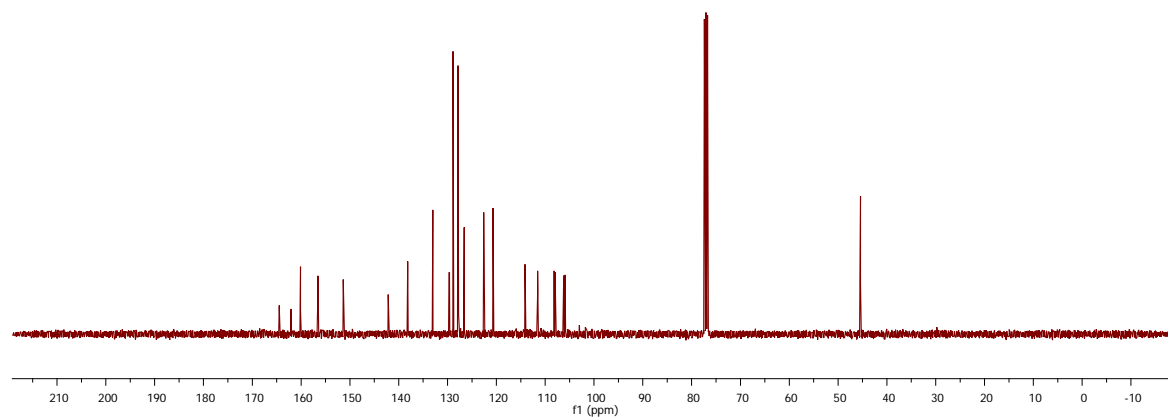
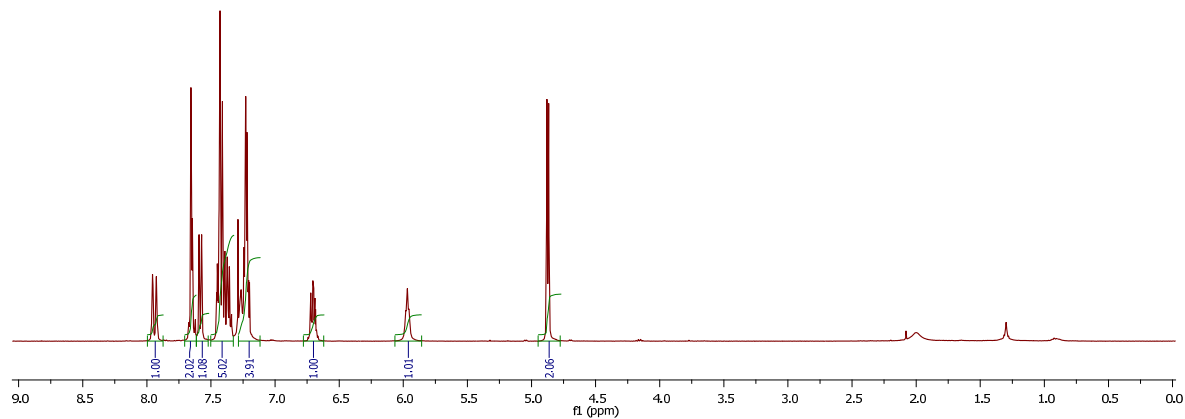
***N*⁴-Benzyl-*N*²-(3-nitrophenyl)quinazoline-2,4-diamine (S73).** Yield: 11.0 mg, 80%. ¹H NMR (400 MHz, CDCl₃) δ 9.03 (t, *J* = 2.2 Hz, 1H), 7.82 – 7.68 (m, 2H), 7.62 (d, *J* = 3.6 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.45 (s, br. 1H), 7.42 – 7.26 (m, 6H), 7.20 (dd, *J* = 3.9, 8.0 Hz, 1H), 5.94 (s, 1H), 4.87 (d, *J* = 5.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 156.3, 151.0, 148.8, 141.6, 137.9, 133.3, 129.3, 128.9, 127.9, 127.9, 126.6, 124.1, 123.0, 120.7, 116.1, 113.4, 111.6, 45.6, 29.7. HRMS (*m/z*): calcd for C₂₁H₁₈N₅O₂ (*M*+*H*) 372.1460; found 372.1462.

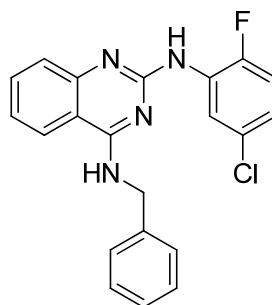




KSC-1-292

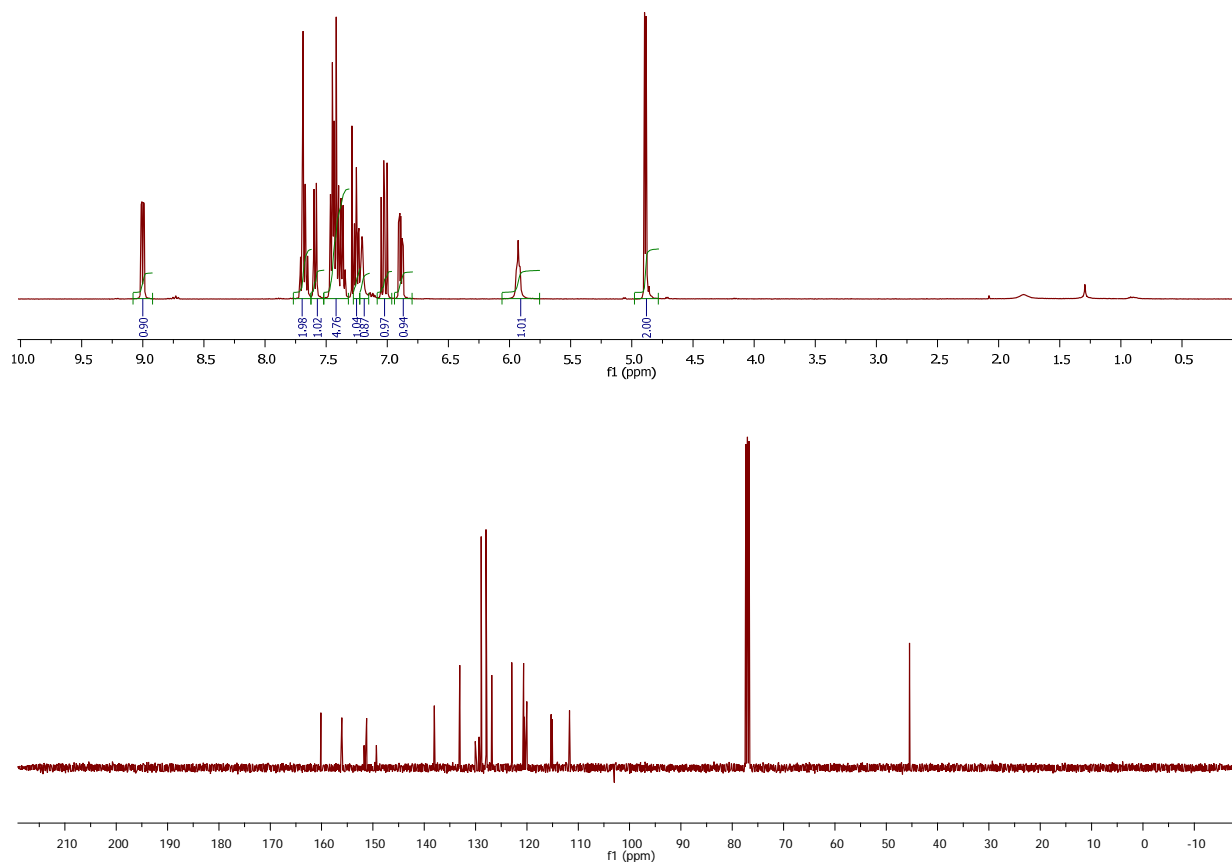
***N*⁴-Benzyl-*N*²-(3-fluorophenyl)quinazoline-2,4-diamine (S74 or 44).** Yield: 58.0 mg, 91%. ¹H NMR (400 MHz, CDCl₃) δ 8.00 – 7.87 (m, 1H), 7.71 – 7.61 (m, 2H), 7.58 (d, *J* = 8.1, 1H), 7.50 – 7.33 (m, 5H), 7.29 – 7.12 (m, 4H), 6.78 – 6.62 (m, 1H), 5.97 (s, br. 1H), 4.87 (d, *J* = 5.3 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.5, 162.1, 160.1, 156.5, 151.4, 142.2, 142.1, 138.2, 133.0, 129.7, 129.6, 128.89, 127.87, 127.8, 126.6, 122.6, 120.7, 114.12, 114.09, 111.6, 108.2, 108.0, 106.2, 105.9, 45.4. HRMS (*m/z*): calcd for C₂₁H₁₈FN₄ (*M*+*H*) 345.1515; found 345.1510.

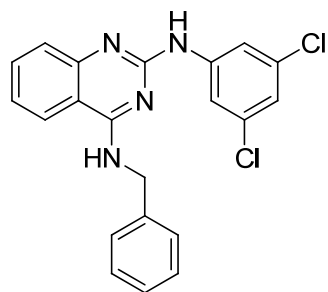




KSC-1-295

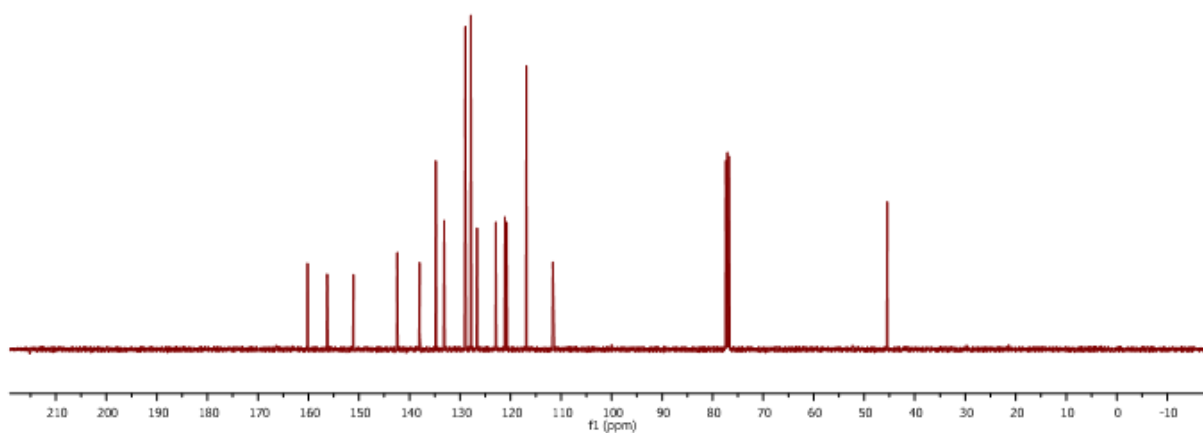
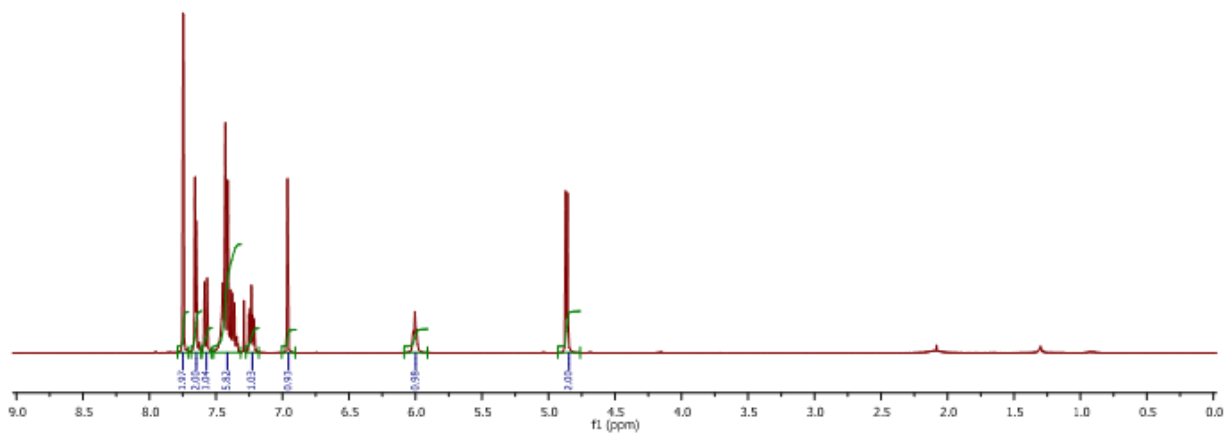
***N*⁴-Benzyl-*N*²-(5-chloro-2-fluorophenyl)quinazoline-2,4-diamine (S75).** Yield: 58.0 mg, 83%. ¹H NMR (400 MHz, CDCl₃) δ 9.00 (dd, *J* = 2.6, 7.3 Hz, 1H), 7.77 – 7.62 (m, 2H), 7.59 (d, *J* = 8.0 Hz, 1H), 7.52 – 7.32 (m, 5H), 7.25 – 7.23 (m, 1H), 7.21 (s, br. 1H), 7.03 (dd, *J* = 8.7, 11.0 Hz, 1H), 6.89 (ddd, *J* = 2.6, 4.3, 8.6 Hz, 1H), 5.93 (s, br. 1H), 4.88 (t, *J* = 7.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.1, 151.7, 151.2, 149.3, 138.1, 133.1, 130.1, 130.0, 129.4, 129.3, 128.9, 128.0, 127.8, 126.8, 123.0, 120.7, 120.53, 120.45, 120.0, 115.3, 115.1, 111.7, 45.5. HRMS (*m/z*): calcd for C₂₁H₁₇ClFN₄ (M+H) 379.1126; found 379.1119.

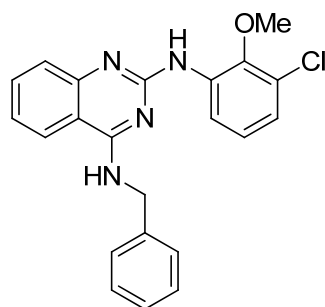




KSC-1-294

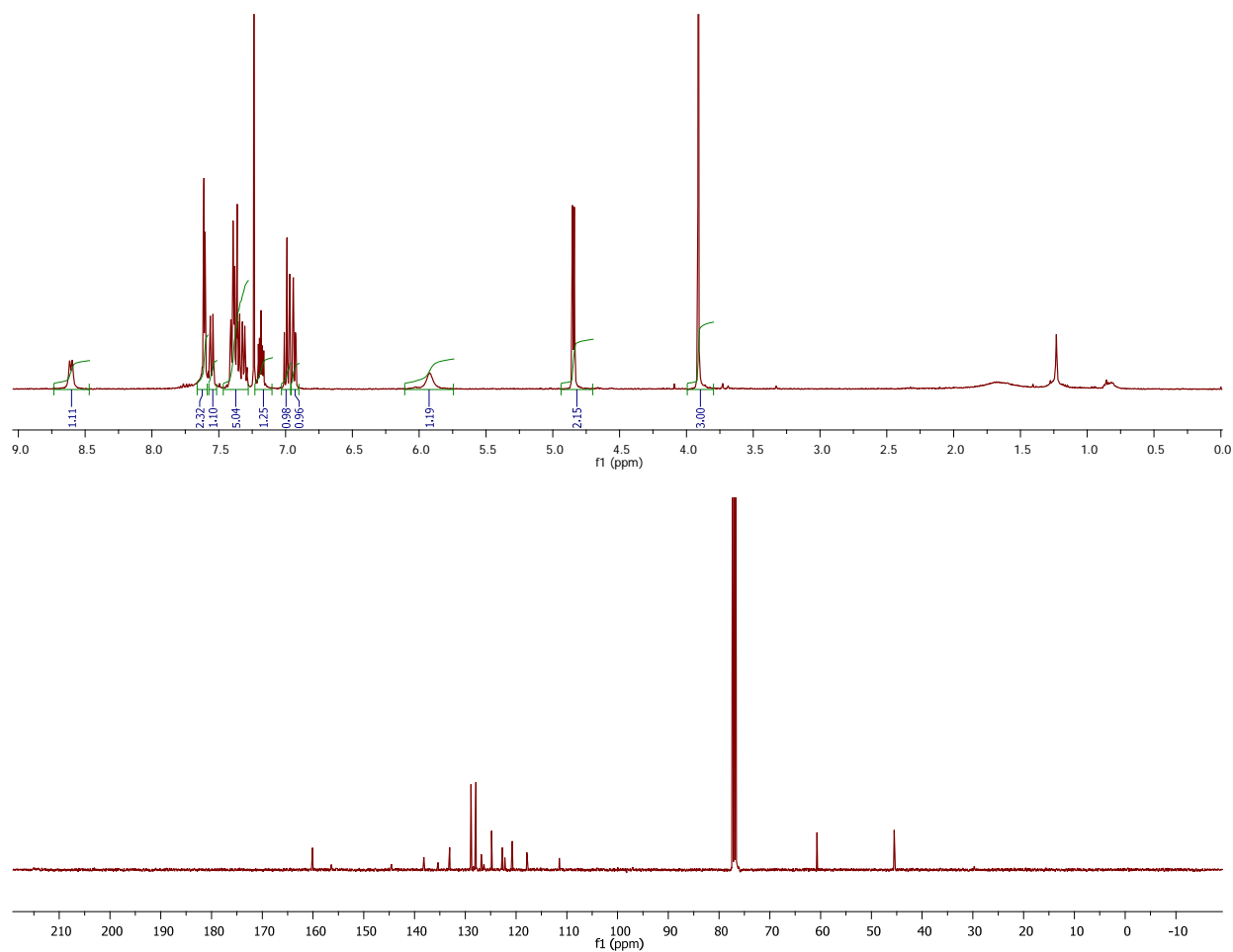
***N*⁴-Benzyl-*N*²-(3,5-dichlorophenyl)quinazoline-2,4-diamine (S76).** Yield: 73.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 7.75 (d, *J* = 1.8 Hz, 2H), 7.69 – 7.61 (m, 2H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.52 – 7.31 (m, 6H), 7.28 – 7.18 (m, 1H), 6.96 (t, *J* = 1.8 Hz, 1H), 6.00 (t, *J* = 5.3 Hz, 1H), 4.86 (d, *J* = 5.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 156.3, 151.1, 142.4, 138.0, 134.8, 133.2, 128.9, 127.9, 127.8, 126.6, 122.9, 121.1, 120.8, 116.9, 111.6, 45.4. HRMS (*m/z*): calcd for C₂₁H₁₇Cl₂N₄ (M+H) 395.0830; found 395.0924.

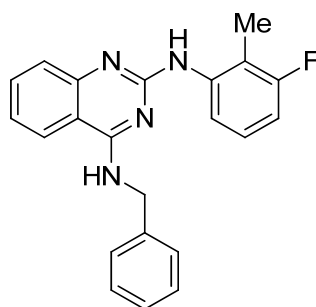




KSC-16-103

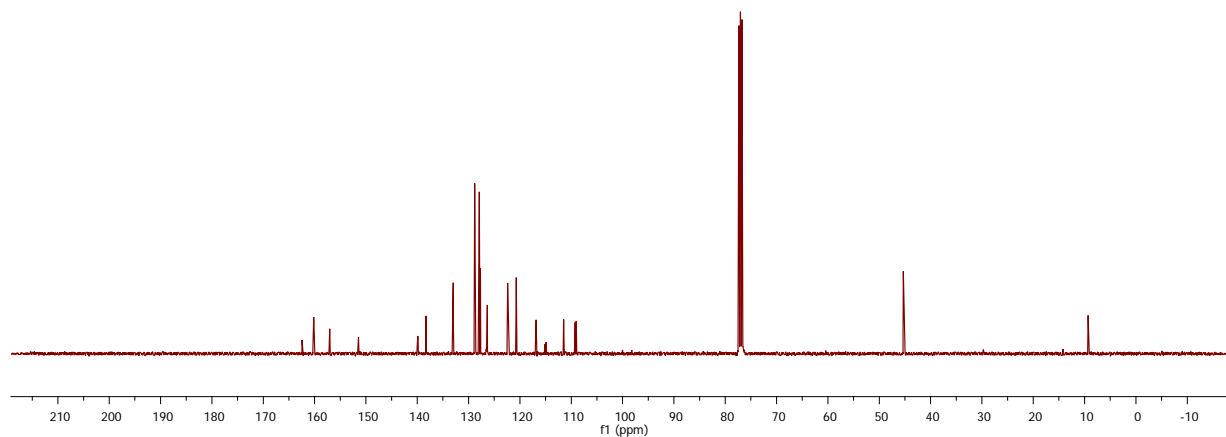
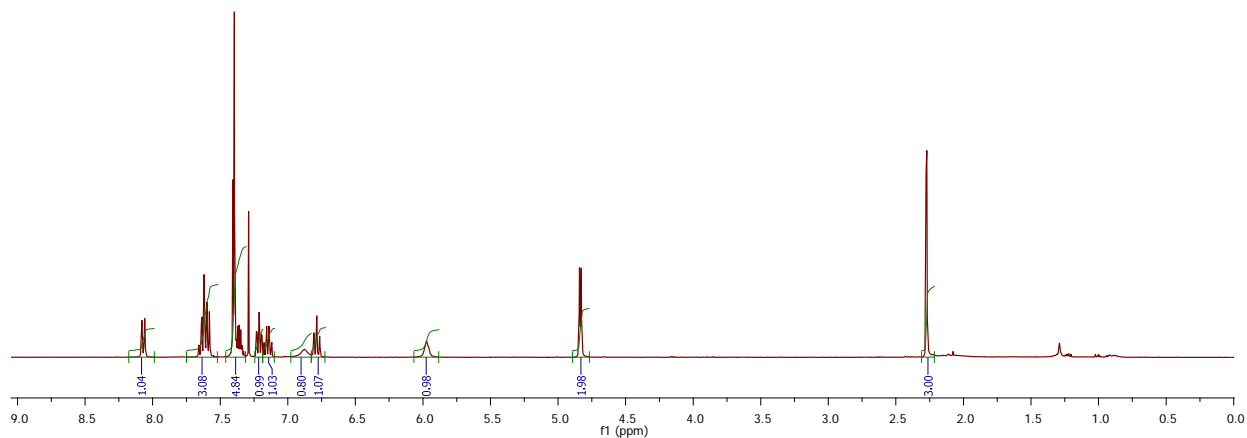
***N*⁴-Benzyl-*N*²-(3-chloro-2-methoxyphenyl)quinazoline-2,4-diamine (S77).** Yield: 6.2 mg, 43%. ¹H NMR (400 MHz, CDCl₃) δ 8.60 (s, 1H), 7.61 (dd, *J* = 1.2, 4.6 Hz, 2H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.47 – 7.28 (m, 5H), 7.23 – 7.10 (m, 1H), 6.99 (t, *J* = 8.1 Hz, 1H), 6.93 (dd, *J* = 1.7, 8.1 Hz, 1H), 5.92 (s, br. 1H), 4.85 (d, *J* = 5.3 Hz, 2H), 3.91 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.4, 144.6, 138.2, 135.4, 133.1, 128.9, 127.9, 127.8, 126.9, 126.3, 124.8, 122.7, 122.2, 120.7, 117.9, 111.5, 60.7, 45.5. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+H) 391.1326; found 391.1324.

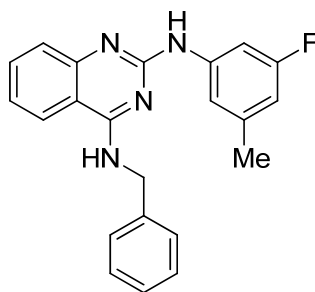




KSC-16-104

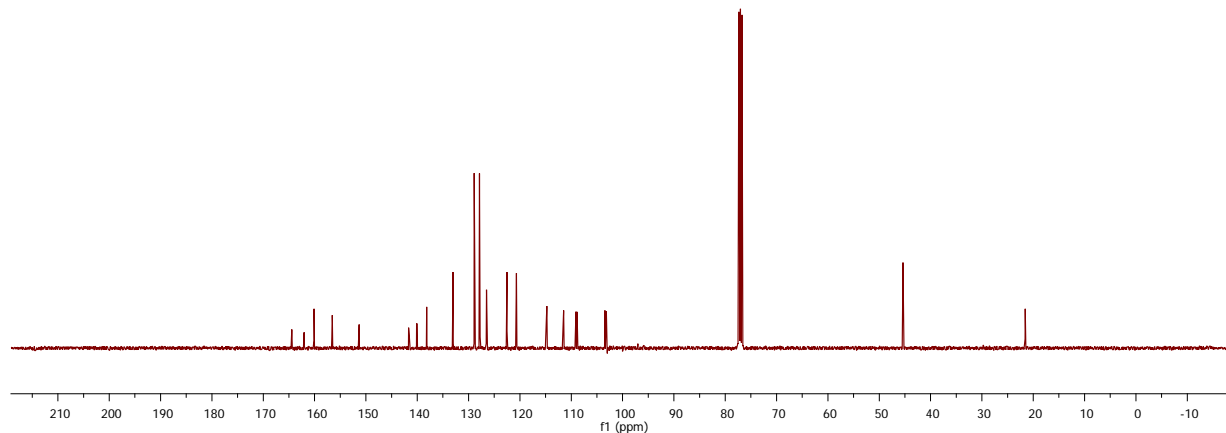
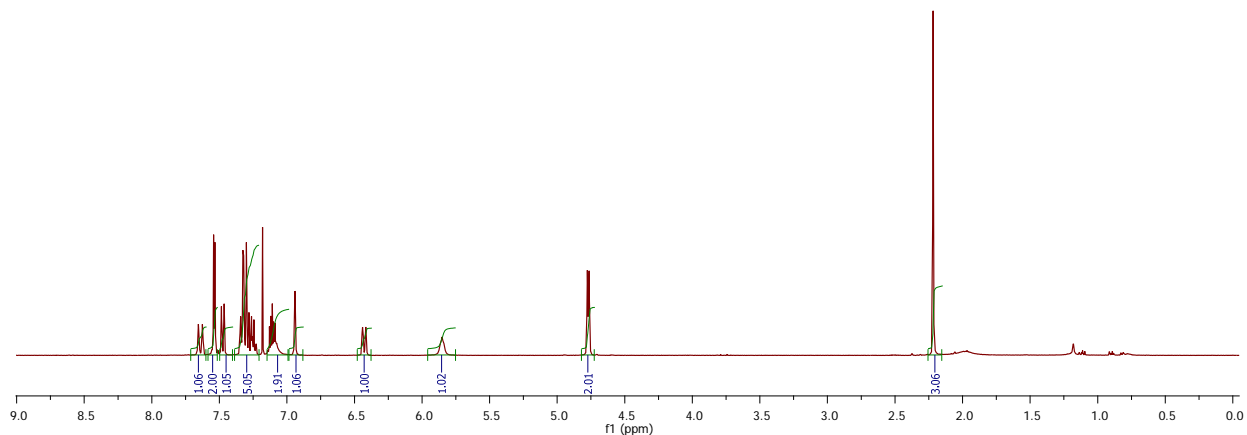
***N*⁴-Benzyl-*N*²-(3-fluoro-2-methylphenyl)quinazoline-2,4-diamine (S78).** Yield: 13.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, *J* = 8.3 Hz, 1H), 7.66 – 7.58 (m, 3H), 7.46 – 7.31 (m, 5H), 7.21 (ddd, *J* = 1.8, 6.3, 8.2 Hz, 1H), 7.15 (dd, *J* = 8.0, 15.0 Hz, 1H), 6.88 (s, br. 1H), 6.79 (t, *J* = 8.5 Hz, 1H), 5.97 (s, br. 1H), 4.84 (d, *J* = 5.2 Hz, 2H), 2.27 (d, *J* = 1.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.4, 160.2, 160.0, 157.1, 151.5, 139.9, 139.9, 138.3, 133.0, 128.8, 127.9, 127.7, 126.5, 126.43, 126.36, 122.4, 120.7, 116.89, 116.86, 115.1, 115.0, 111.5, 109.3, 109.0, 45.3, 9.32, 9.26. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (M+H) 359.1672; found 359.1677.

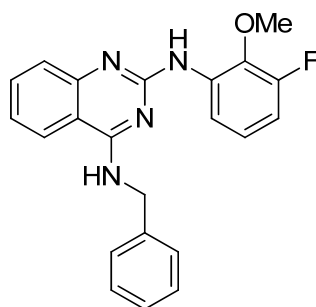




KSC-16-105

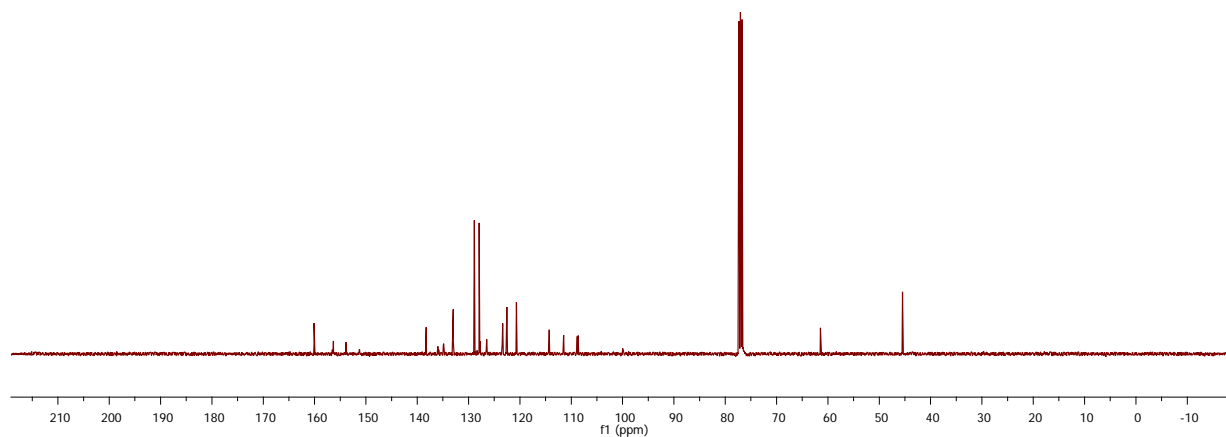
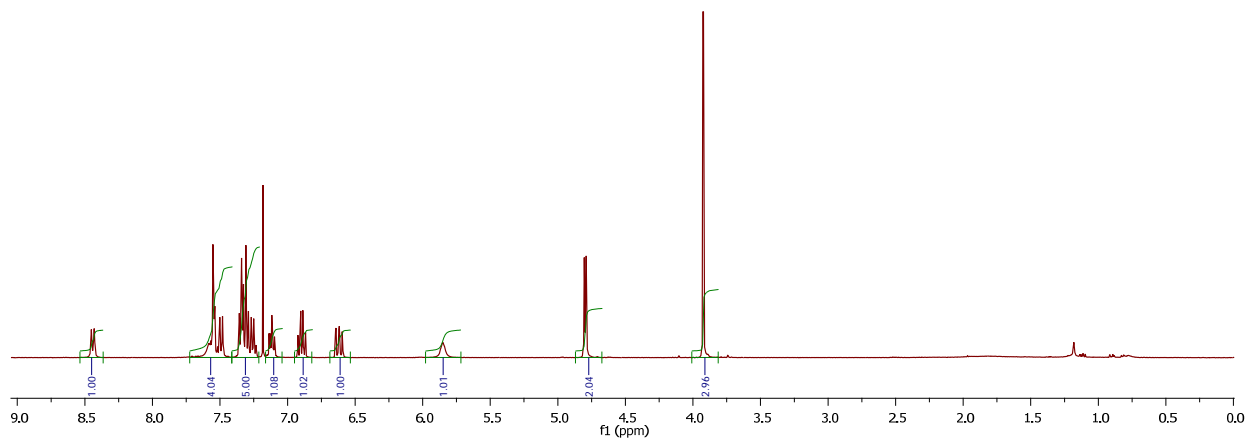
***N*⁴-Benzyl-*N*²-(3-fluoro-5-methylphenyl)quinazoline-2,4-diamine (S79).** Yield: 13.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.64 (d, *J* = 11.6 Hz, 1H), 7.54 (d, *J* = 3.5 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.39 – 7.21 (m, 5H), 7.15 – 6.99 (m, 2H), 6.94 (s, 1H), 6.43 (d, *J* = 9.3 Hz, 1H), 5.85 (s, br. 1H), 4.77 (d, *J* = 5.0 Hz, 2H), 2.22 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 164.4, 162.0, 160.1, 156.5, 151.3, 141.7, 141.6, 140.1, 140.0, 138.2, 133.0, 128.9, 127.9, 127.8, 126.5, 122.5, 120.7, 114.74, 114.72, 111.5, 109.1, 108.9, 103.4, 103.2, 103.0, 45.4, 21.58, 21.56. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1675.

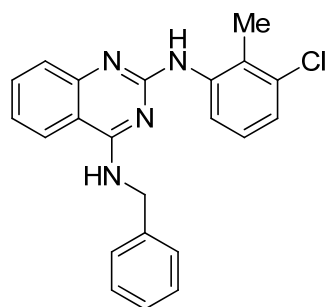




KSC-16-106

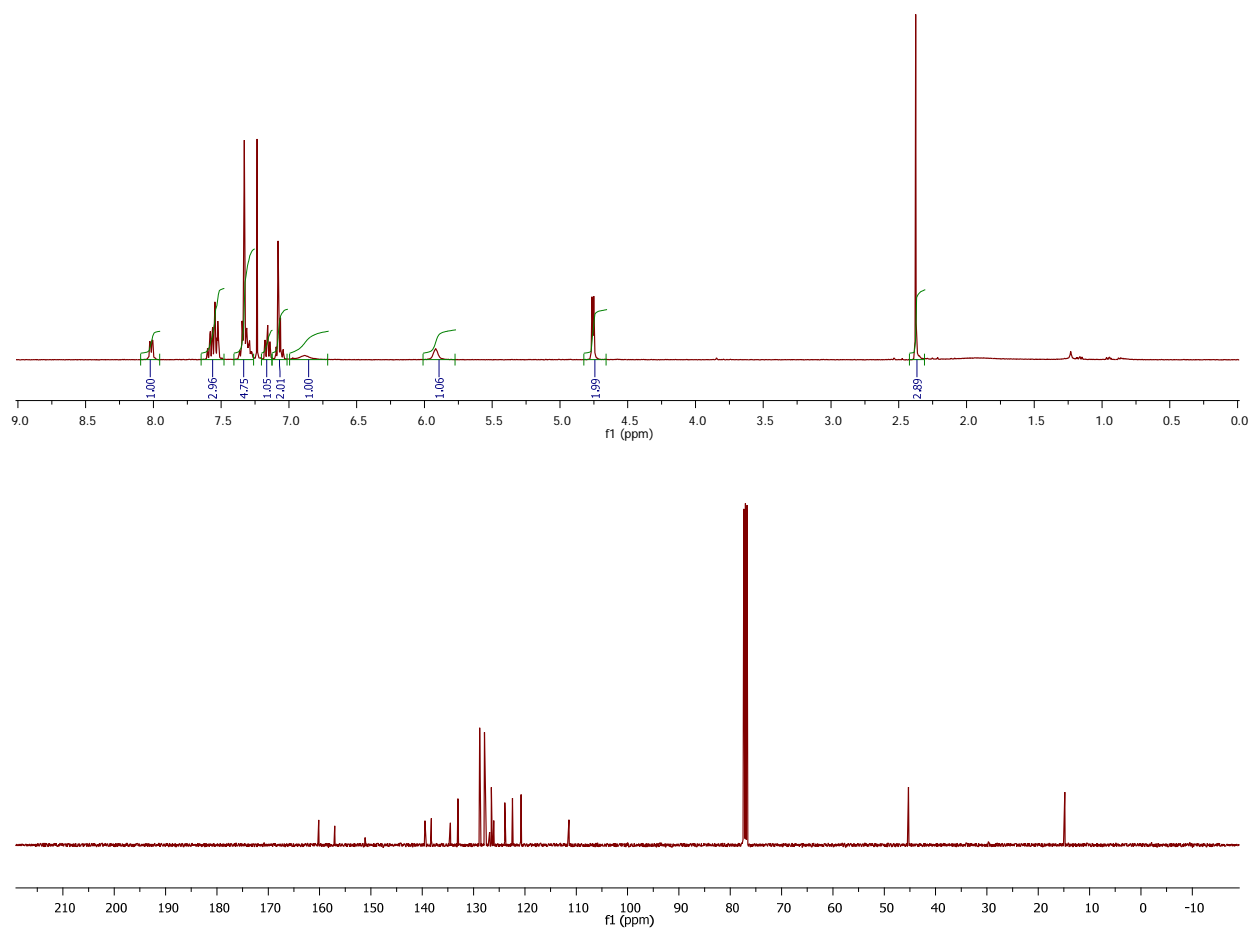
***N*⁴-Benzyl-*N*²-(3-fluoro-2-methoxyphenyl)quinazoline-2,4-diamine (S80).** Yield: 12.4 mg, 89%. ¹H NMR (400 MHz, CDCl₃) δ 8.44 (d, *J* = 8.4 Hz, 1H), 7.72 – 7.41 (m, 4H), 7.41 – 7.21 (m, 5H), 7.12 (ddd, *J* = 2.8, 5.3, 8.2 Hz, 1H), 6.89 (td, *J* = 6.0, 8.4 Hz, 1H), 6.62 (ddd, *J* = 1.5, 8.4, 11.2 Hz, 1H), 5.85 (s, br. 1H), 4.80 (d, *J* = 5.3 Hz, 2H), 3.92 (d, *J* = 1.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 156.3, 153.9, 151.2, 138.2, 136.0, 135.8, 134.9, 134.9, 133.0, 128.9, 127.9, 127.8, 126.5, 123.5, 123.4, 122.6, 120.7, 114.3, 111.5, 108.8, 108.6, 61.5, 61.4, 45.5. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄O (*M*+H) 375.1621; found 375.1624.

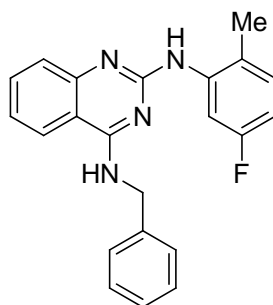




KSC-16-107

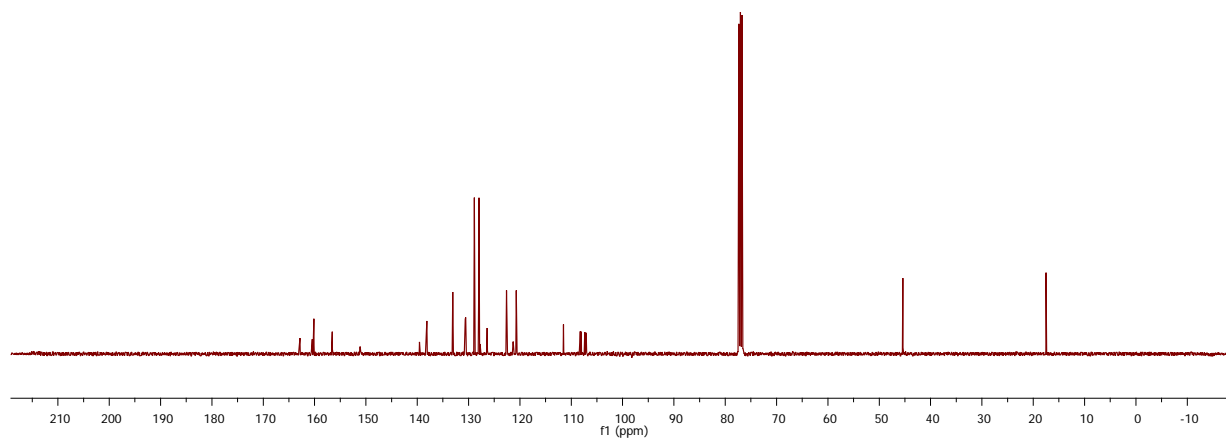
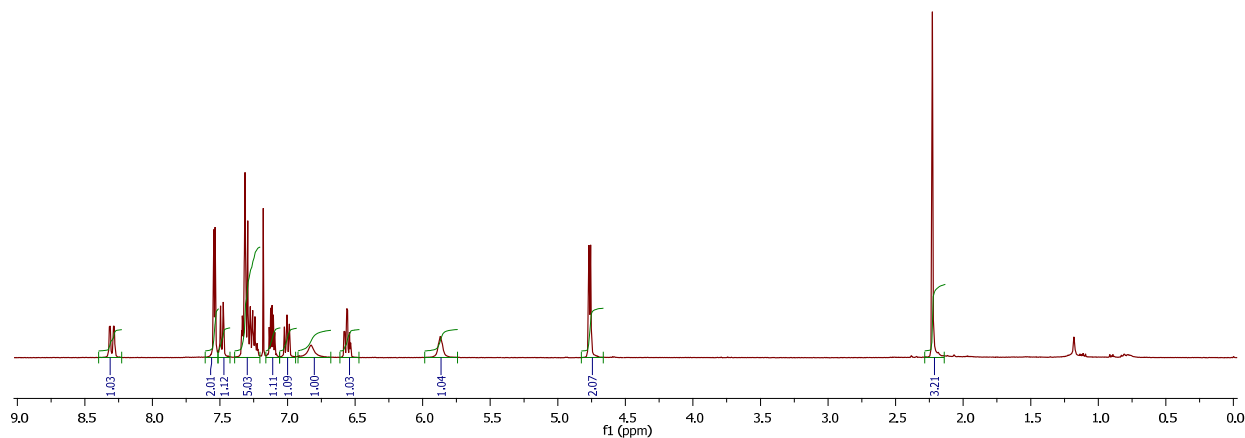
***N*⁴-Benzyl-*N*²-(3-chloro-2-methylphenyl)quinazoline-2,4-diamine (S81).** Yield: 11.7 mg, 84%. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (dd, *J* = 2.6, 6.7 Hz, 1H), 7.60 – 7.53 (m, 3H), 7.41 – 7.26 (m, 5H), 7.16 (ddd, *J* = 1.5, 6.6, 8.2 Hz, 1H), 7.12 – 7.01 (m, 2H), 7.00 – 6.71 (s, br. 1H), 5.92 (s, br. 1H), 4.76 (d, *J* = 5.2 Hz, 2H), 2.38 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 157.1, 151.1, 139.5, 138.2, 134.5, 133.1, 128.8, 127.9, 127.7, 126.9, 126.5, 126.1, 123.9, 122.4, 120.8, 120.7, 111.4, 45.3, 14.8. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+*H*) 375.1376; found 375.1378.

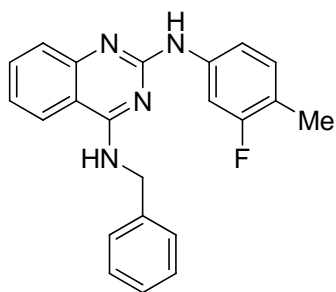




KSC-16-108

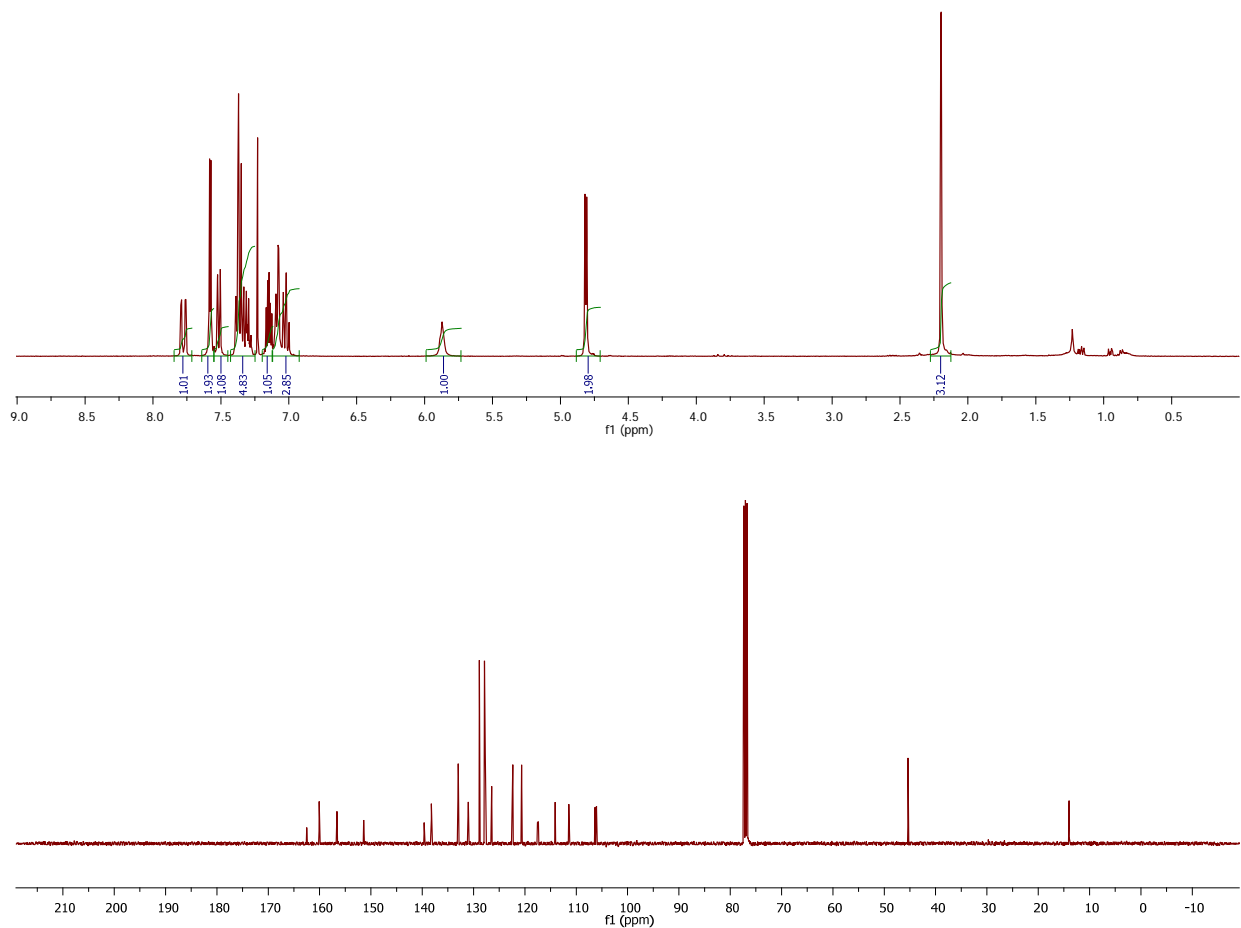
***N*⁴-Benzyl-*N*²-(5-fluoro-2-methylphenyl)quinazoline-2,4-diamine (S82).** Yield: 12.7 mg, 96%. ¹H NMR (400 MHz, CDCl₃) δ 8.30 (dd, *J* = 2.6, 12.1 Hz, 1H), 7.54 (d, *J* = 3.6 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 1H), 7.39 – 7.20 (m, 5H), 7.11 (dt, *J* = 4.1, 8.2 Hz, 1H), 7.06 – 6.94 (m, 1H), 6.83 (s, br. 1H), 6.56 (td, *J* = 2.7, 8.2 Hz, 1H), 5.87 (s, br. 1H), 4.76 (d, *J* = 5.2 Hz, 2H), 2.23 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.8, 160.5, 160.1, 156.6, 151.1, 139.6, 139.4, 138.1, 133.1, 130.7, 130.6, 128.9, 128.0, 127.8, 126.4, 122.6, 121.3, 120.7, 111.5, 108.3, 108.0, 107.4, 107.1, 45.4, 17.5. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (M+H) 359.1672; found 359.1678.

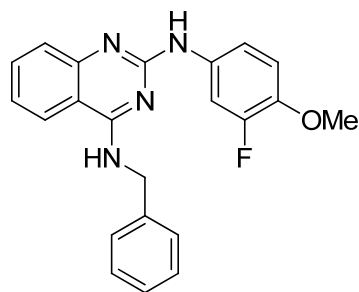




KSC-16-109

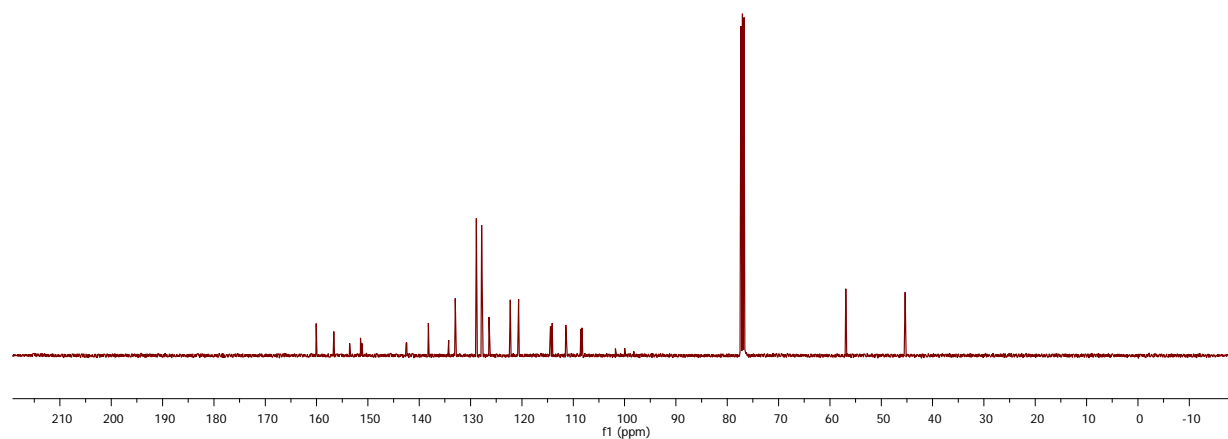
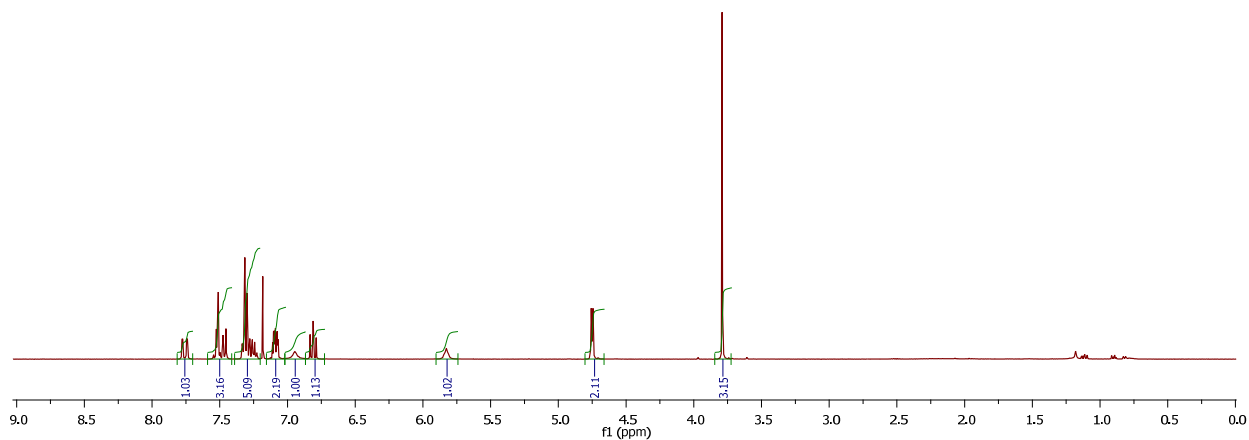
***N*⁴-Benzyl-*N*²-(3-fluoro-4-methylphenyl)quinazoline-2,4-diamine (S83).** Yield: 13.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (dd, *J* = 2.1, 12.4, 1H), 7.64 – 7.55 (m, 2H), 7.51 (d, *J* = 8.1, 1H), 7.43 – 7.25 (m, 5H), 7.20 – 7.12 (m, 1H), 7.12 – 6.92 (m, 3H), 5.87 (s, br. 1H), 4.81 (d, *J* = 5.2 Hz, 2H), 2.20 (d, *J* = 1.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 160.11, 160.08, 156.6, 151.4, 139.6, 139.5, 138.2, 133.0, 131.02, 130.95, 128.9, 127.9, 127.7, 126.5, 122.4, 120.7, 117.6, 117.4, 114.14, 114.11, 111.5, 106.3, 106.1, 45.4, 14.02, 13.99. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1673.

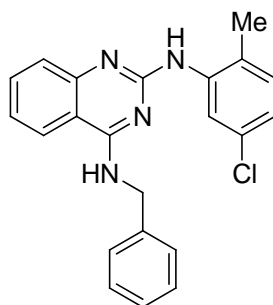




KSC-16-110

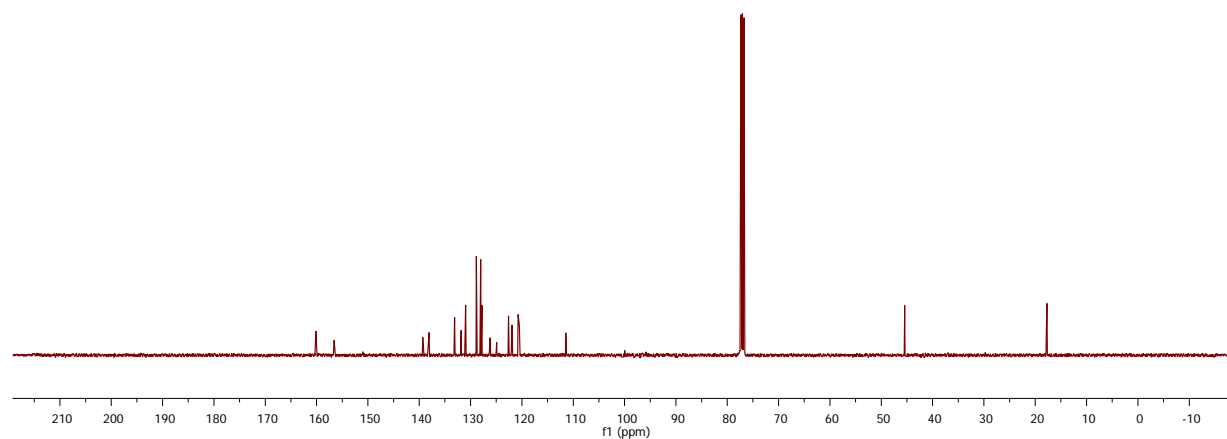
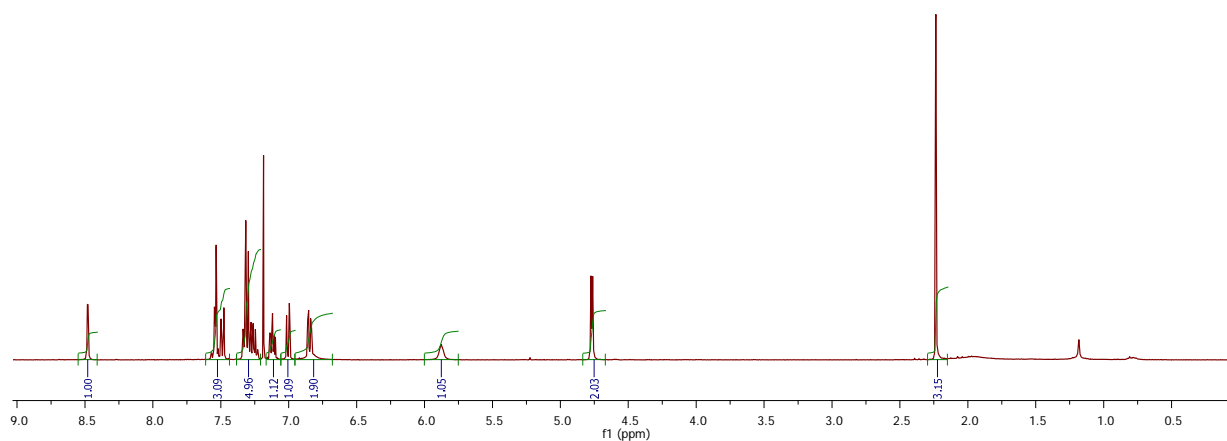
***N*⁴-Benzyl-*N*²-(3-fluoro-4-methoxyphenyl)quinazoline-2,4-diamine (S84).** Yield: 13.0 mg, 94%. ¹H NMR (400 MHz, CDCl₃) δ 7.76 (dd, *J* = 2.6, 13.8 Hz, 1H), 7.59 – 7.41 (m, 3H), 7.39 – 7.20 (m, 5H), 7.16 – 7.02 (m, 2H), 6.95 (s, br. 1H), 6.81 (t, *J* = 9.1 Hz, 1H), 5.83 (s, br. 1H), 4.75 (d, *J* = 5.2 Hz, 2H), 3.79 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.7, 153.6, 151.4, 151.2, 142.6, 142.4, 138.2, 134.4, 134.3, 133.0, 128.9, 127.9, 127.7, 126.4, 122.3, 120.7, 114.4, 114.4, 114.1, 114.1, 111.5, 108.5, 108.3, 56.9, 45.3. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄O (*M*+H) 375.1621; found 375.1623.

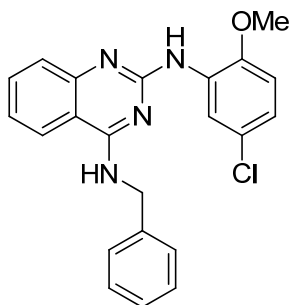




KSC-16-112

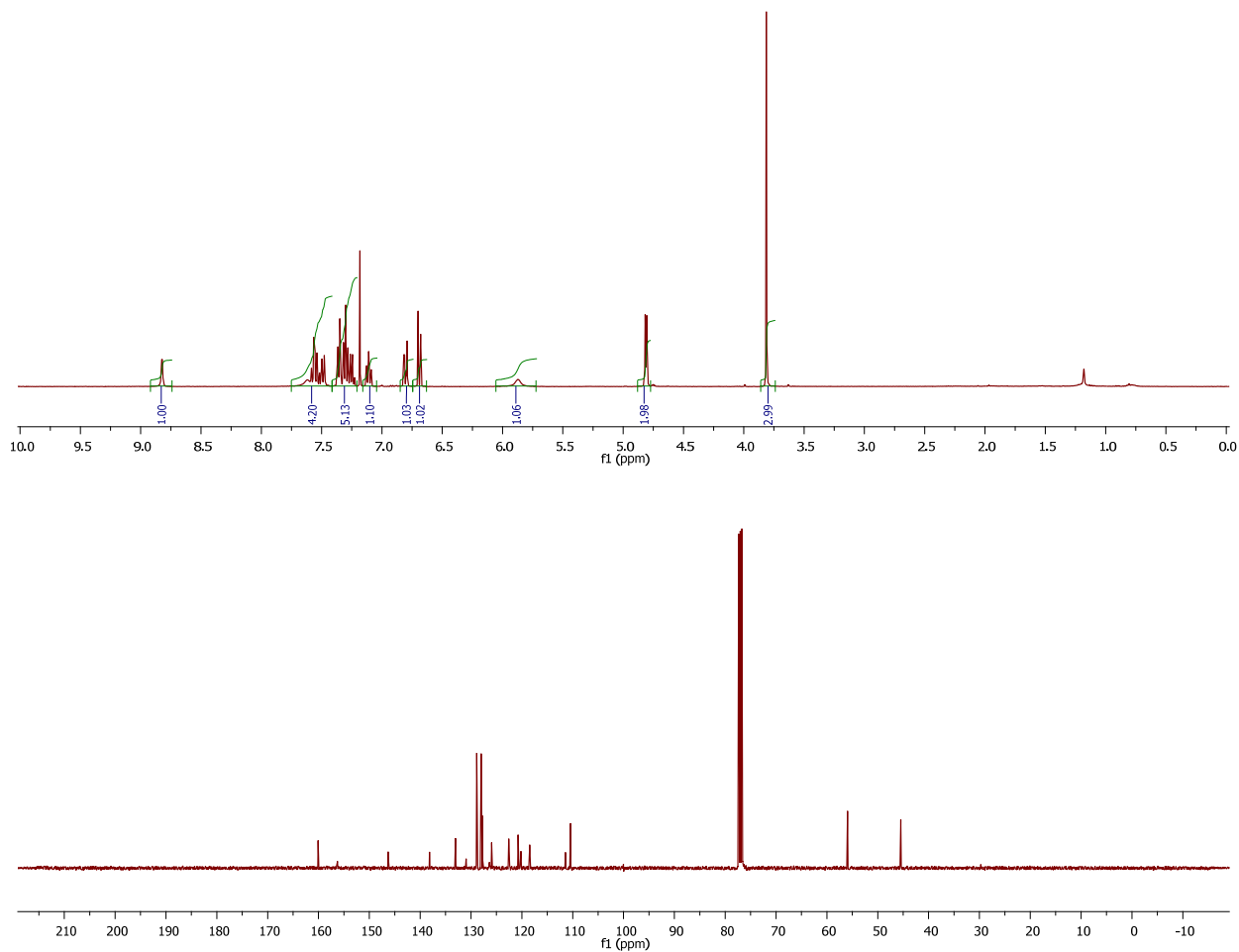
***N*⁴-Benzyl-*N*²-(5-chloro-2-methylphenyl)quinazoline-2,4-diamine (S85).** Yield: 10.6 mg, 76%. ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, *J* = 2.1 Hz, 1H), 7.61 – 7.44 (m, 3H), 7.38 – 7.21 (m, 5H), 7.12 (ddd, *J* = 2.8, 5.3, 8.2 Hz, 1H), 7.01 (d, *J* = 8.1 Hz, 1H), 6.85 (dd, *J* = 2.2, 8.0 Hz, 2H), 5.88 (s, br. 1H), 4.77 (d, *J* = 5.1 Hz, 2H), 2.24 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 156.6, 139.3, 138.1, 133.1, 131.8, 131.0, 128.9, 128.0, 127.8, 126.2, 124.9, 122.6, 121.9, 120.7, 120.5, 111.5, 45.4, 17.7. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+H) 375.1376; found 375.1379.

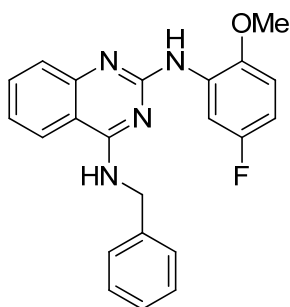




KSC-16-113

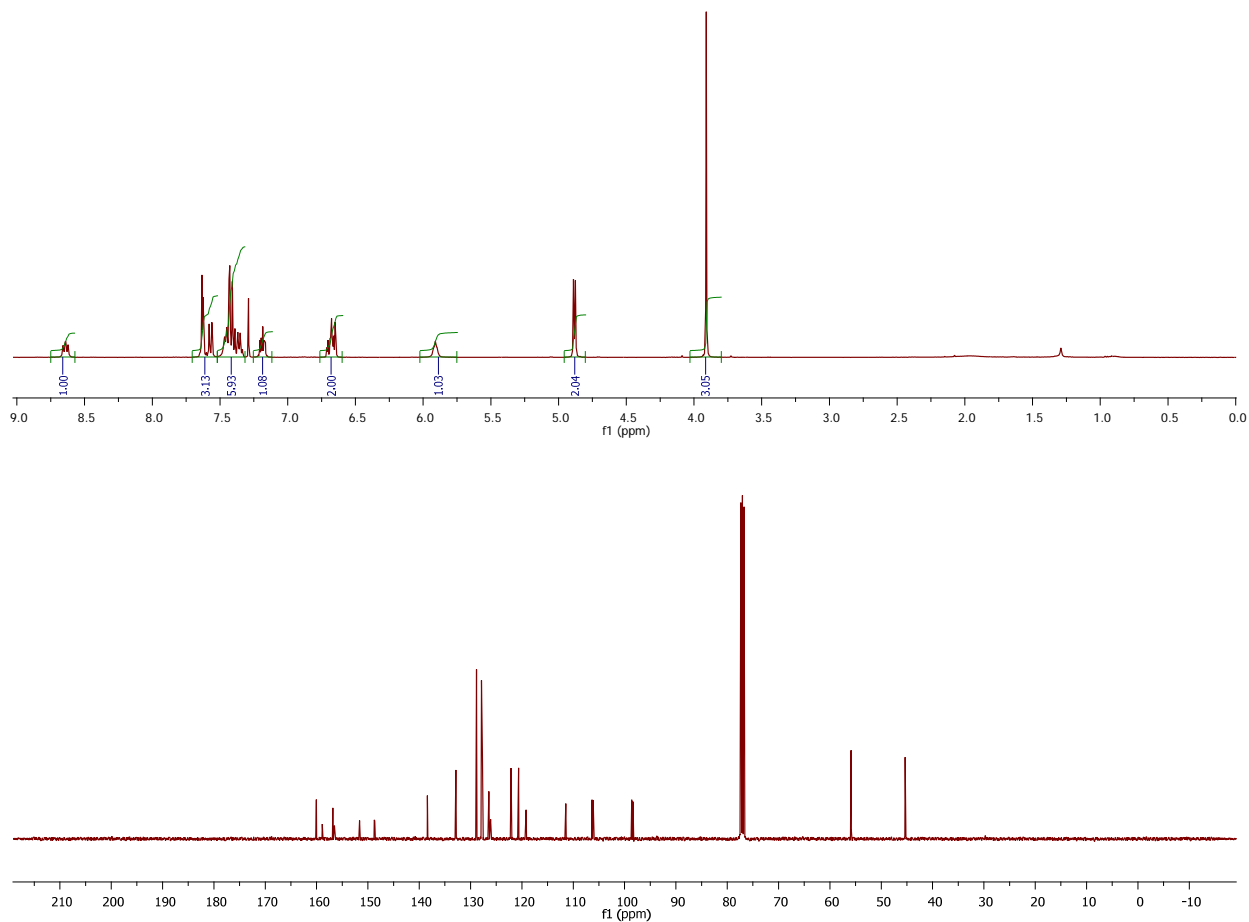
***N*⁴-Benzyl-*N*²-(5-chloro-2-methoxyphenyl)quinazoline-2,4-diamine (S86).** Yield: 11.0 mg, 76%. ¹H NMR (400 MHz, CDCl₃) δ 8.83 (s, 1H), 7.75 – 7.41 (m, 4H), 7.41 – 7.21 (m, 5H), 7.11 (ddd, *J* = 1.7, 6.5, 8.2 Hz, 1H), 6.80 (dd, *J* = 2.6, 8.6 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 1H), 5.87 (s, br, 1H), 4.81 (d, *J* = 5.3 Hz, 2H), 3.81 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.3, 146.3, 138.2, 133.0, 131.0, 128.9, 128.0, 127.8, 126.4, 125.9, 122.6, 120.7, 120.2, 118.5, 111.4, 110.4, 56.0, 45.5. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+*H*) 391.1326; found 391.1324.

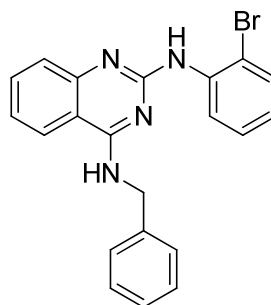




KSC-16-120

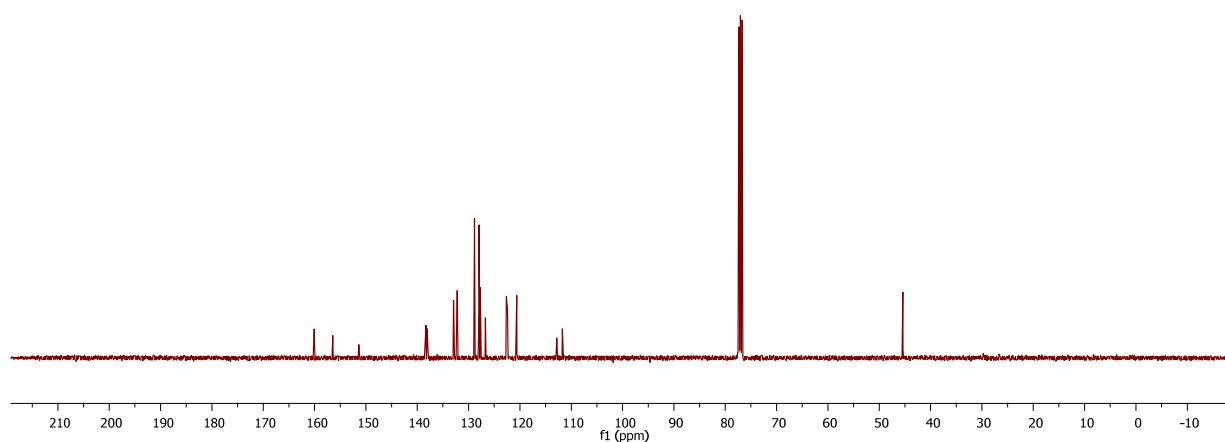
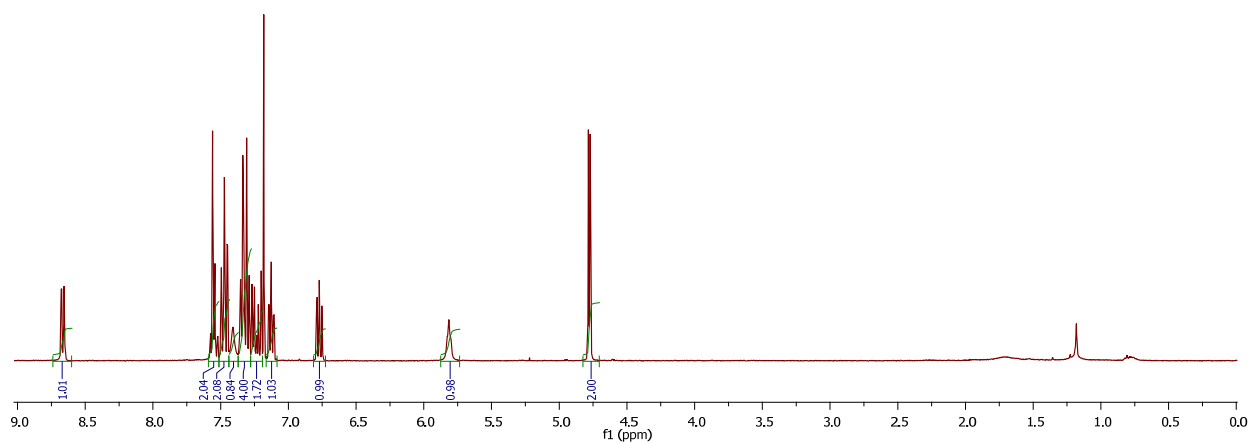
***N*⁴-Benzyl-*N*²-(5-fluoro-2-methoxyphenyl)quinazoline-2,4-diamine (S87).** Yield: 13.0 mg, 94%. ¹H NMR (400 MHz, CDCl₃) δ 8.75 – 8.57 (m, 1H), 7.71 – 7.52 (m, 3H), 7.40 (qdd, *J* = 5.5, 8.0, 13.6 Hz, 6H), 7.18 (ddd, *J* = 3.3, 4.8, 8.2 Hz, 1H), 6.76 – 6.60 (m, 2H), 5.91 (s, br. 1H), 4.88 (d, *J* = 5.4 Hz, 2H), 3.91 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 158.9, 156.8, 156.5, 151.6, 148.8, 148.7, 138.4, 132.9, 128.8, 127.9, 127.7, 126.5, 126.14, 126.11, 122.1, 120.7, 119.3, 119.2, 111.4, 106.4, 106.1, 98.6, 98.4, 55.9, 45.4. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄O (*M*+*H*) 375.1621; found 375.1622.

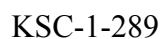


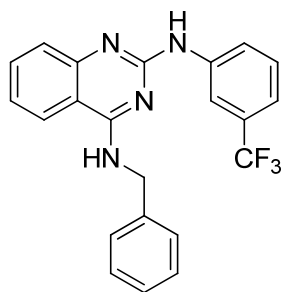


KSC-1-288

***N*⁴-Benzyl-*N*²-(2-bromophenyl)quinazoline-2,4-diamine (S88).** Yield: 18.0 mg, 60%. ¹H NMR (400 MHz, CDCl₃) δ 8.67 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.51 – 7.44 (m, 2H), 7.41 (s, br. 1H), 7.37 – 7.28 (m, 4H), 7.28 – 7.19 (m, 2H), 7.13 (ddd, *J* = 2.3, 5.8, 8.2 Hz, 1H), 6.81 – 6.73 (m, 1H), 5.81 (s, br. 1H), 4.78 (d, *J* = 5.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.4, 138.3, 138.1, 132.9, 132.2, 128.9, 128.0, 127.9, 127.7, 126.7, 122.7, 122.4, 120.7, 120.6, 112.8, 111.7, 45.4. HRMS (*m/z*): calcd for C₂₁H₁₈BrN₄ (M+H) 405.0715 and 407.0694; found 407.0688.

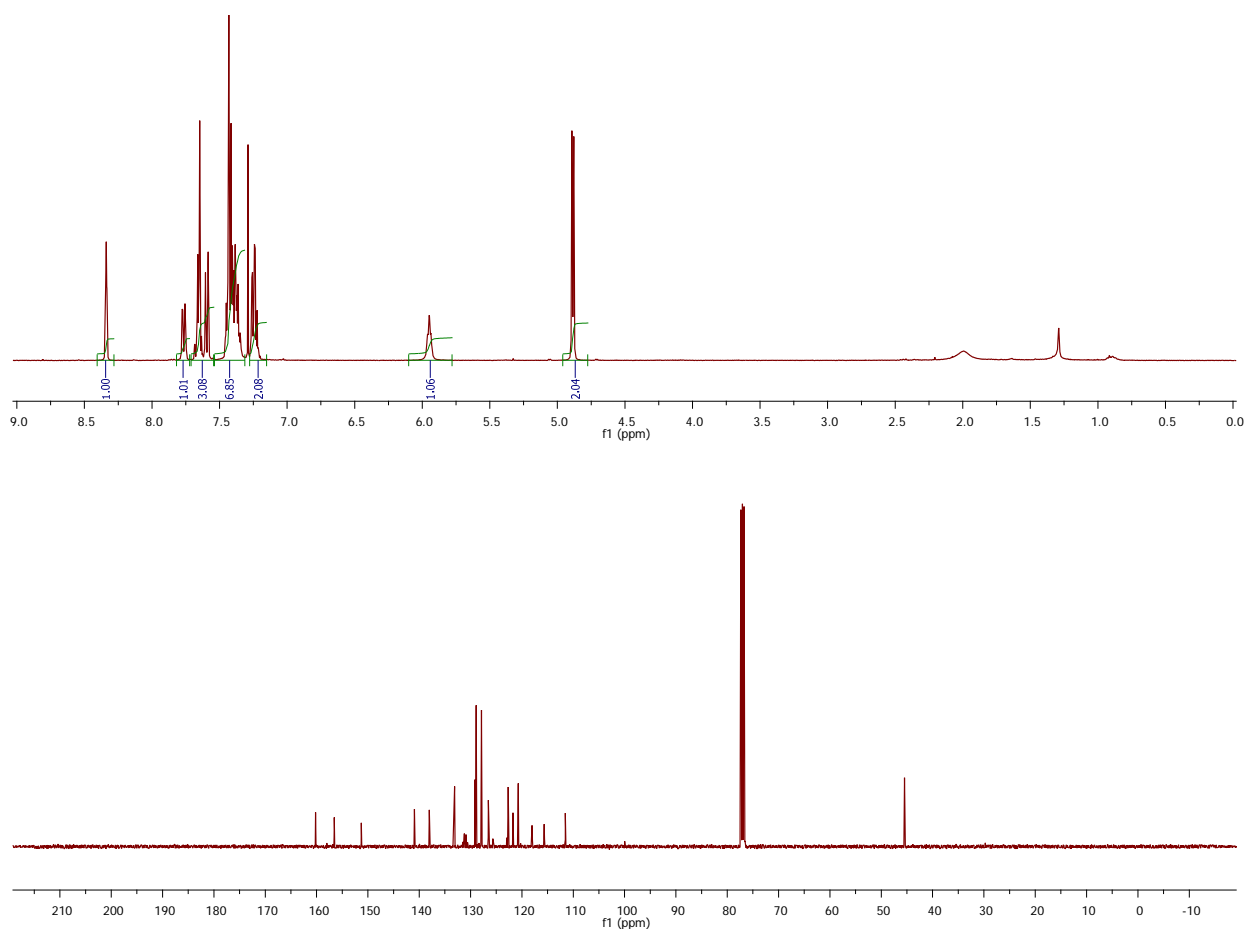


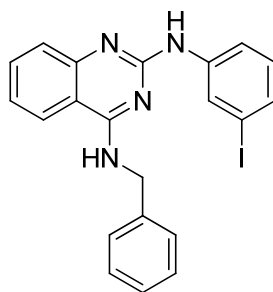




KSC-16-150

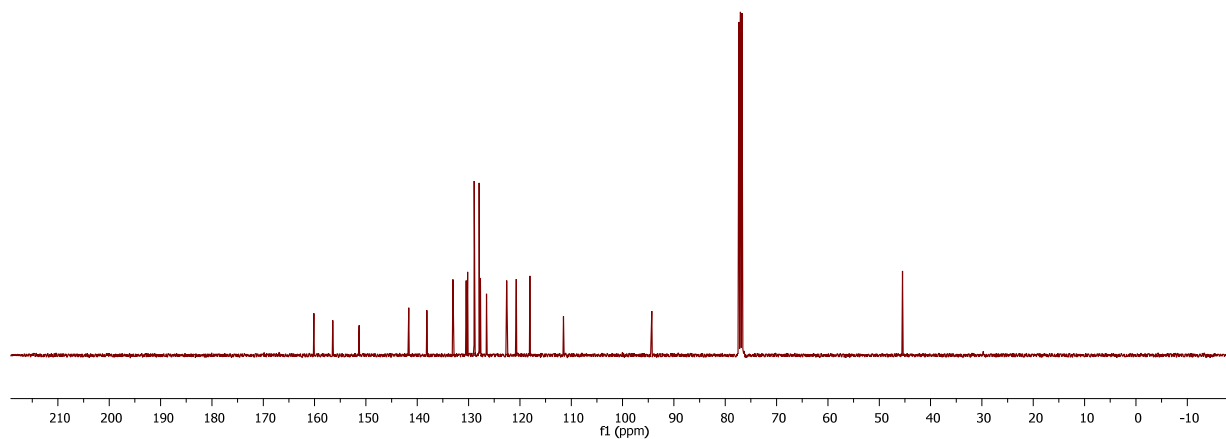
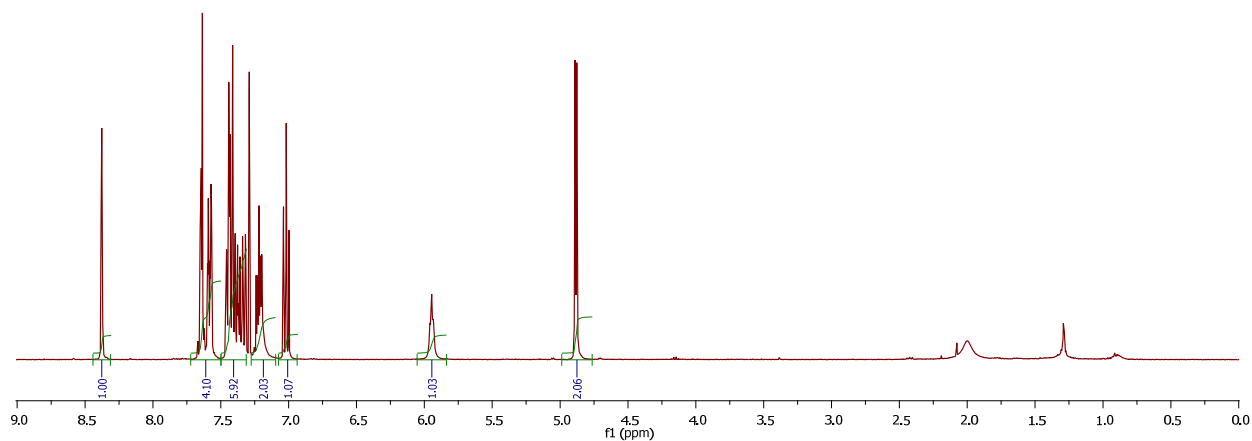
***N*⁴-Benzyl-*N*²-(3-(trifluoromethyl)phenyl)quinazoline-2,4-diamine (S90).** Yield: 14.6 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.34 (s, 1H), 7.77 (d, *J* = 8.2 Hz, 1H), 7.71 – 7.54 (m, 3H), 7.54 – 7.31 (m, 7H), 7.24 (ddd, *J* = 2.4, 5.0, 8.2 Hz, 2H), 5.95 (s, br. 1H), 4.89 (d, *J* = 5.3 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 156.5, 151.3, 140.9, 138.0, 133.1, 131.5, 131.2, 130.9, 130.5, 129.1, 128.9, 127.9, 127.8, 126.5, 125.7, 123.0, 122.7, 121.7, 120.7, 118.1, 118.04, 118.00, 117.97, 115.7, 115.66, 115.62, 115.58, 111.6, 45.5. HRMS (*m/z*): calcd for C₂₂H₁₈F₃N₄ (*M*+*H*) 395.1484; found 395.1481.

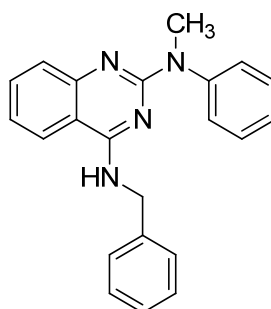




KSC-16-152

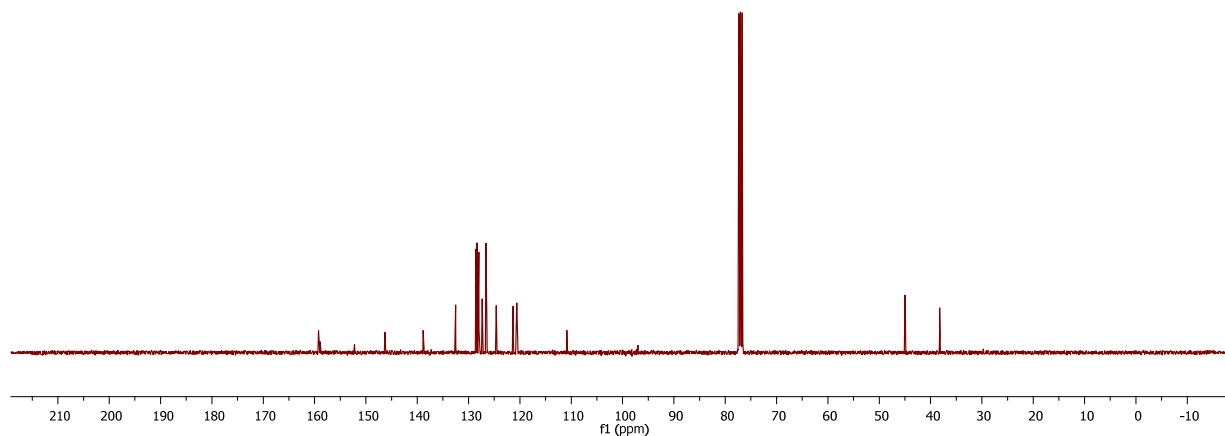
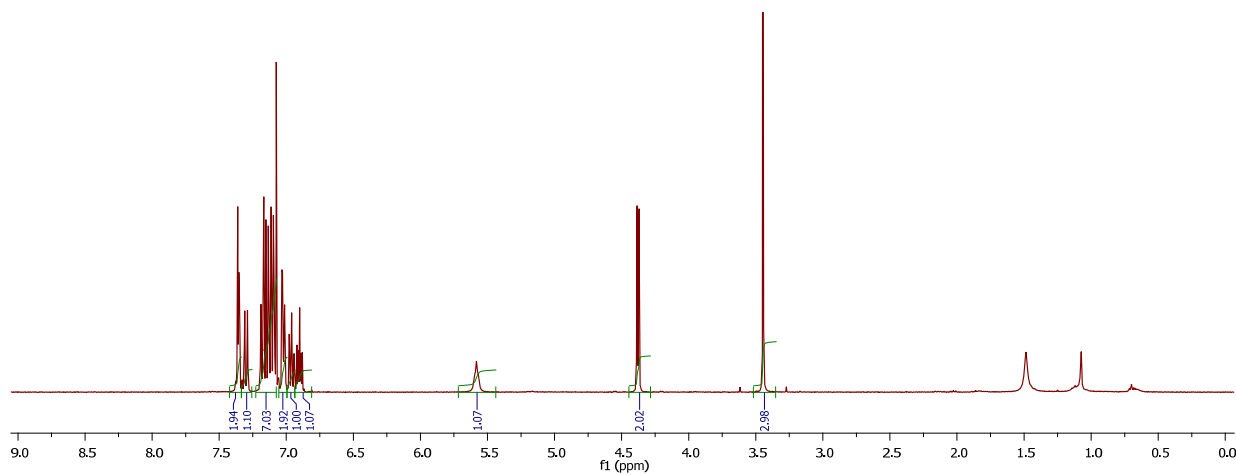
***N*⁴-Benzyl-*N*²-(3-iodophenyl)quinazoline-2,4-diamine (S91).** Yield: 16.0 mg, 95%. ¹H NMR (400 MHz, CDCl₃) δ 8.38 (t, *J* = 1.9 Hz, 1H), 7.62 (tdd, *J* = 4.1, 5.9, 9.2 Hz, 4H), 7.50 – 7.31 (m, 6H), 7.22 (ddd, *J* = 3.0, 5.2, 8.2 Hz, 2H), 7.02 (t, *J* = 8.0 Hz, 1H), 5.95 (s, 1H), 4.88 (d, *J* = 5.3 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.3, 141.6, 138.1, 133.1, 130.5, 130.2, 128.9, 127.9, 127.8, 127.7, 126.5, 122.6, 120.7, 118.1, 111.5, 94.3, 45.5. HRMS (*m/z*): calcd for C₂₁H₁₈IN₄ (*M*+*H*) 453.0576; found 453.0571.

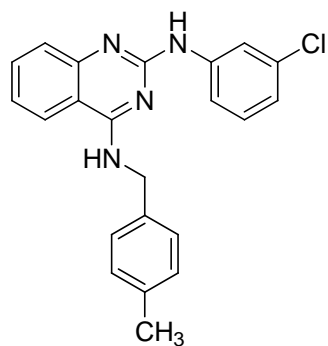




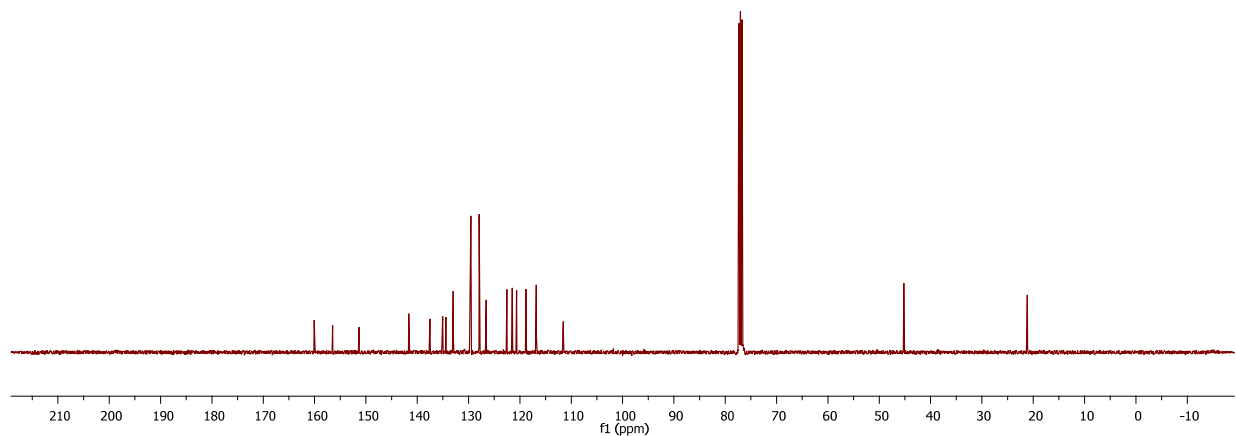
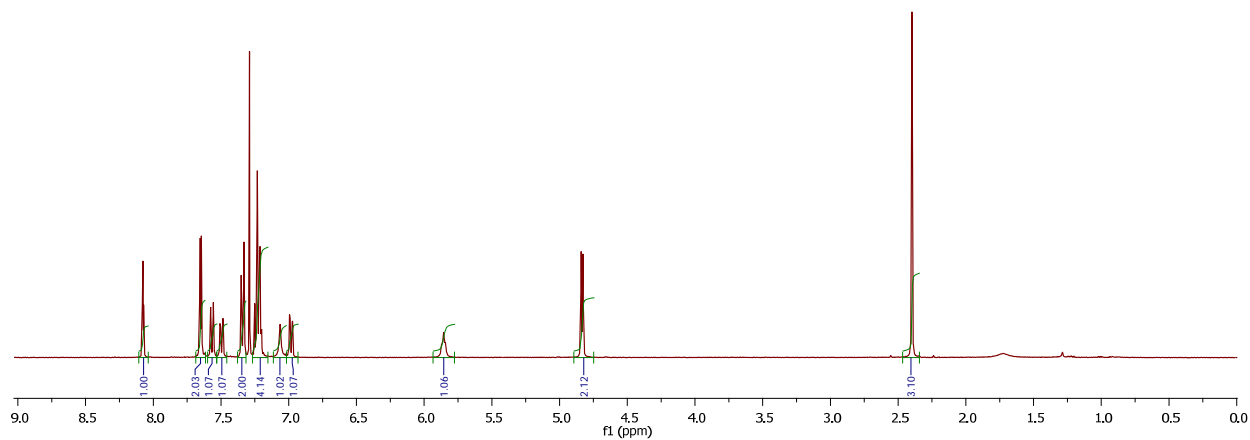
KSC-16-188

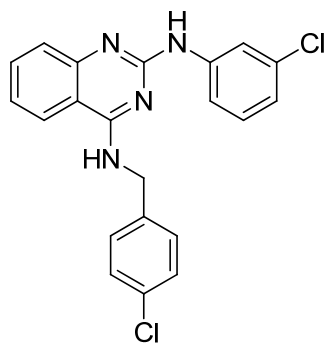
***N*⁴-Benzyl-*N*²-methyl-*N*²-phenylquinazoline-2,4-diamine (S92).** Yield: 7.7 mg, 61%. ¹H NMR (400 MHz, CDCl₃) δ 7.36 (dd, *J* = 1.3, 4.6 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.26 – 7.09 (m, 7H), 7.05 – 7.00 (m, 2H), 7.00 – 6.94 (m, 1H), 6.90 (ddd, *J* = 3.3, 4.9, 8.2 Hz, 1H), 5.58 (s, 1H), 4.38 (d, *J* = 5.6 Hz, 2H), 3.45 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.2, 158.9, 152.2, 146.3, 138.9, 132.5, 128.6, 128.4, 128.0, 127.3, 126.6, 126.5, 124.6, 121.3, 120.6, 110.9, 45.0, 38.2. HRMS (*m/z*): calcd for C₂₂H₂₁N₄ (*M*+*H*) 341.1766; found 341.1766.





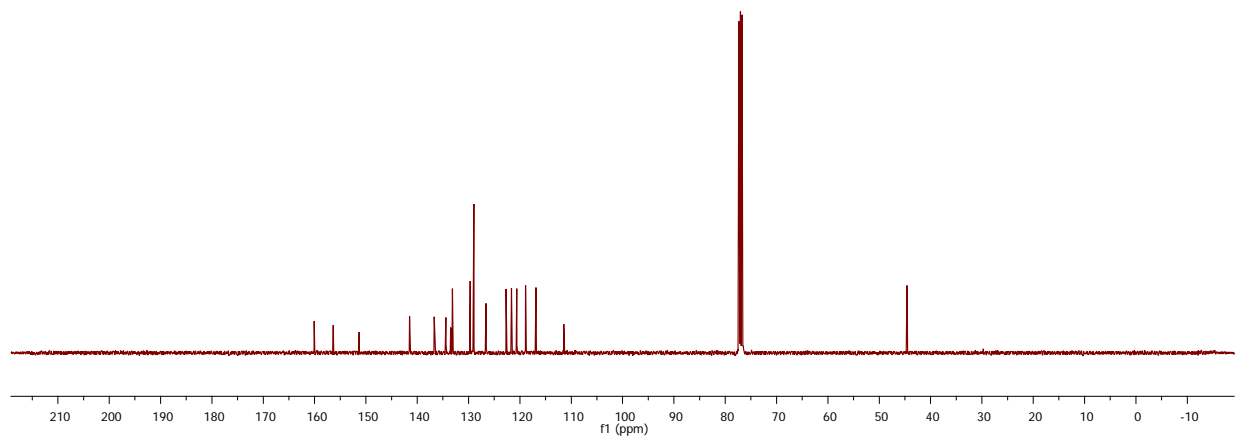
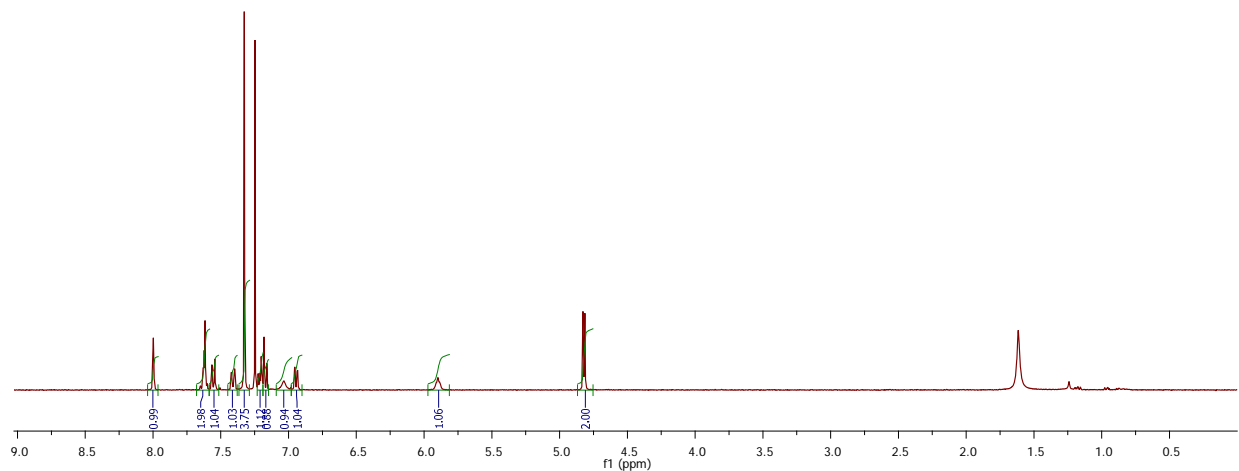
***N*²-(3-Chlorophenyl)-*N*⁴-(4-methylbenzyl)quinazoline-2,4-diamine (S93).** Yield: 13.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.08 (t, *J* = 2.0 Hz, 1H), 7.65 (d, *J* = 3.5 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.20 (m, 4H), 7.06 (s, br. 1H), 6.98 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H), 5.86 (s, br. 1H), 4.83 (d, *J* = 5.3 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.3, 141.7, 137.6, 135.1, 134.4, 133.0, 129.7, 129.6, 127.9, 126.6, 122.6, 121.5, 120.7, 118.8, 116.8, 111.6, 45.2, 21.2. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (M+H) 375.1376; found 375.1376.

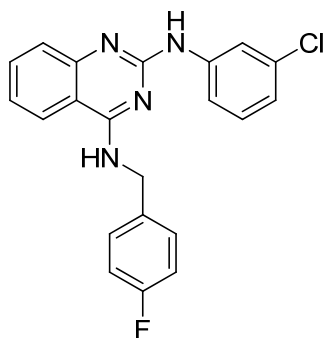




KSC-16-89

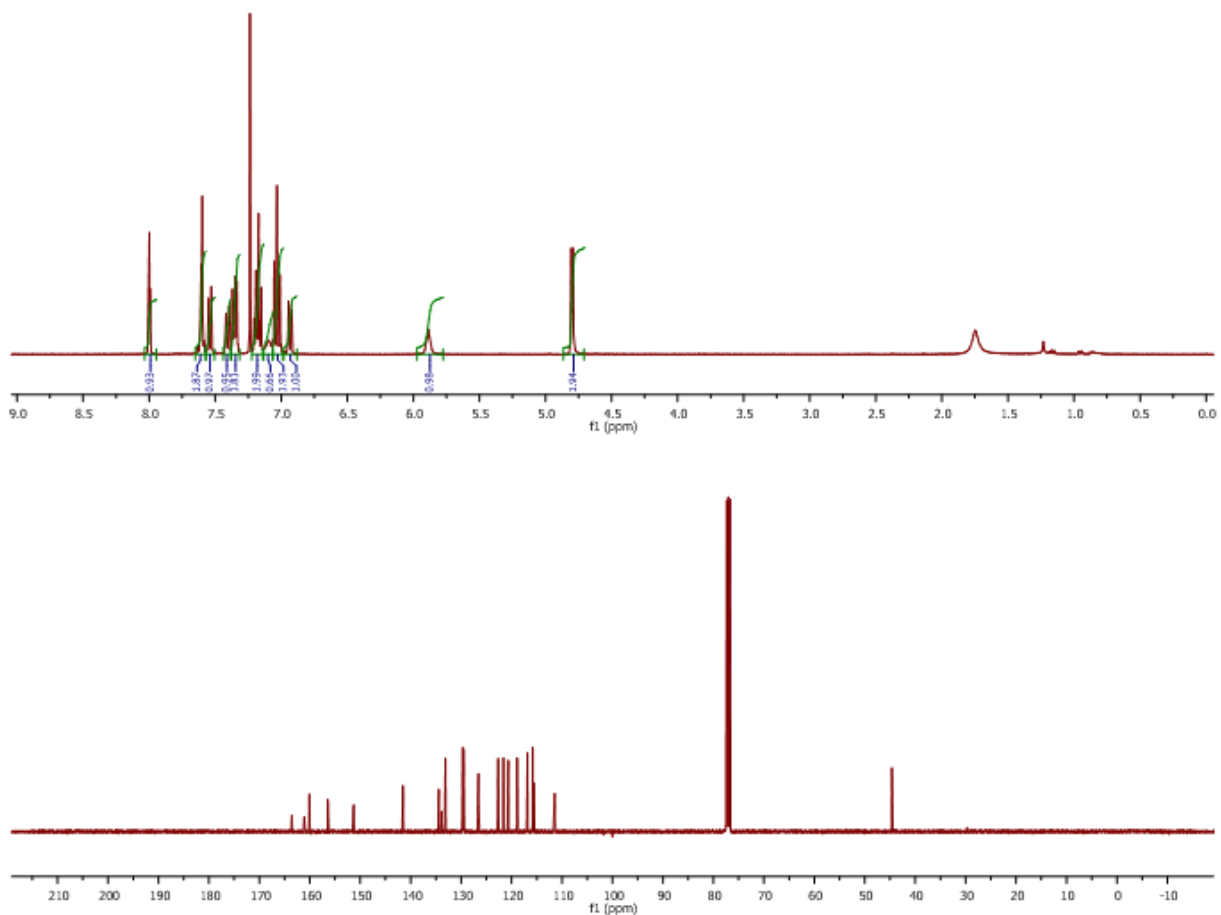
***N*⁴-(4-Chlorobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S94).** Yield: 13.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (t, *J* = 2.0 Hz, 1H), 7.63 – 7.61 (m, 2H), 7.55 (d, *J* = 8.2, 1H), 7.45 – 7.38 (m, 1H), 7.33 (s, 4H), 7.22 – 7.19 (m, 1H), 7.17 (d, *J* = 8.1 Hz, 1H), 7.03 (s, br. 1H), 6.94 (dd, *J* = 1.1, 7.9 Hz, 1H), 5.90 (s, br. 1H), 4.82 (d, *J* = 5.6 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.4, 151.3, 141.5, 136.7, 134.4, 133.5, 133.2, 129.7, 129.1, 129.0, 126.6, 122.7, 121.6, 120.6, 118.9, 116.9, 111.4, 44.6. HRMS (*m/z*): calcd for C₂₁H₁₇Cl₂N₄ (*M*+*H*) 395.0830; found 395.0826.

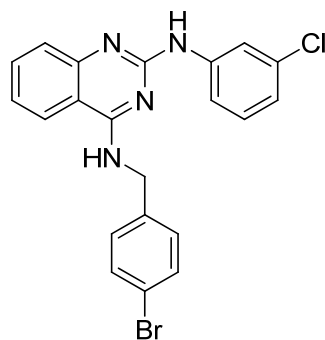




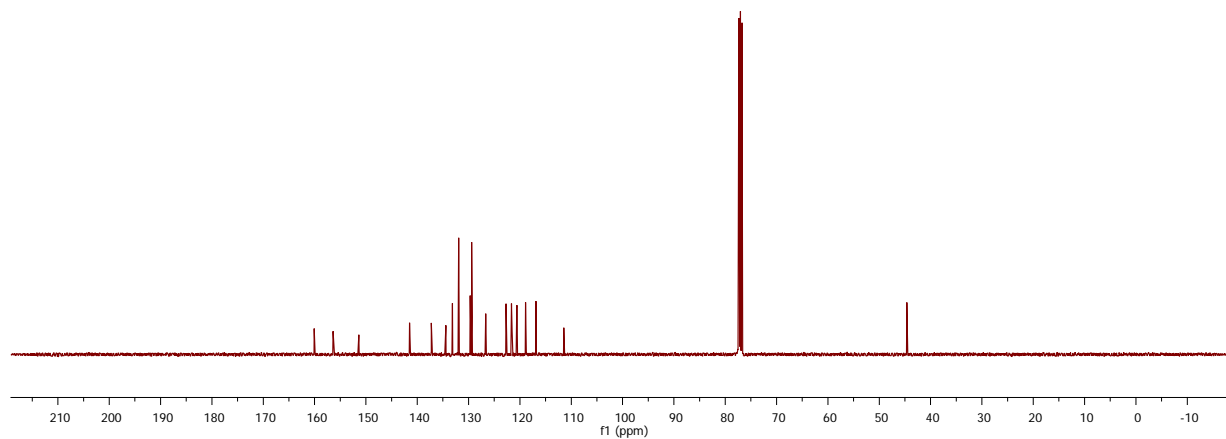
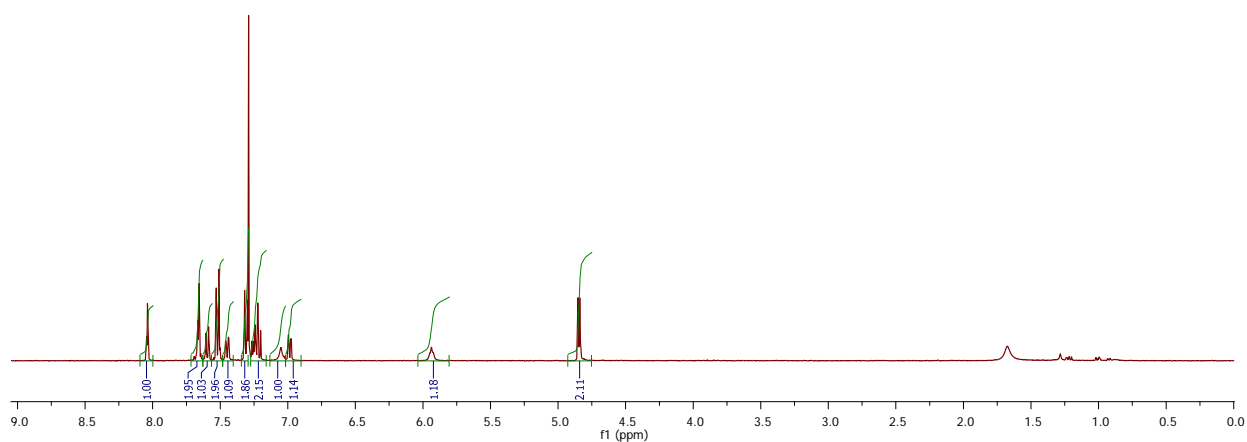
KSC-16-98

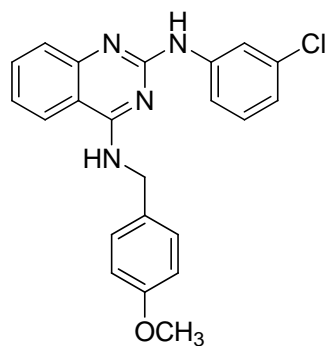
***N*²-(3-Chlorophenyl)-*N*⁴-(4-fluorobenzyl)quinazoline-2,4-diamine (S95 or 12).** Yield: 13.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 8.00 (t, *J* = 2.0 Hz, 1H), 7.65 – 7.57 (m, 2H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.44 – 7.38 (m, 1H), 7.35 (dd, *J* = 5.3, 8.7 Hz, 2H), 7.22 – 7.14 (m, 2H), 7.09 (s, br. 1H), 7.06 – 6.99 (m, 2H), 6.93 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H), 5.89 (s, br. 1H), 4.80 (d, *J* = 5.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 163.6, 161.1, 160.1, 156.4, 151.3, 141.6, 134.4, 133.93, 133.90, 133.1, 130.0, 129.54, 129.46, 126.6, 122.7, 121.6, 120.7, 118.9, 116.9, 115.8, 115.6, 111.5, 44.6. HRMS (*m/z*): calcd for C₂₁H₁₇ClFN₄ (*M*+*H*) 379.1126; found 379.1123.





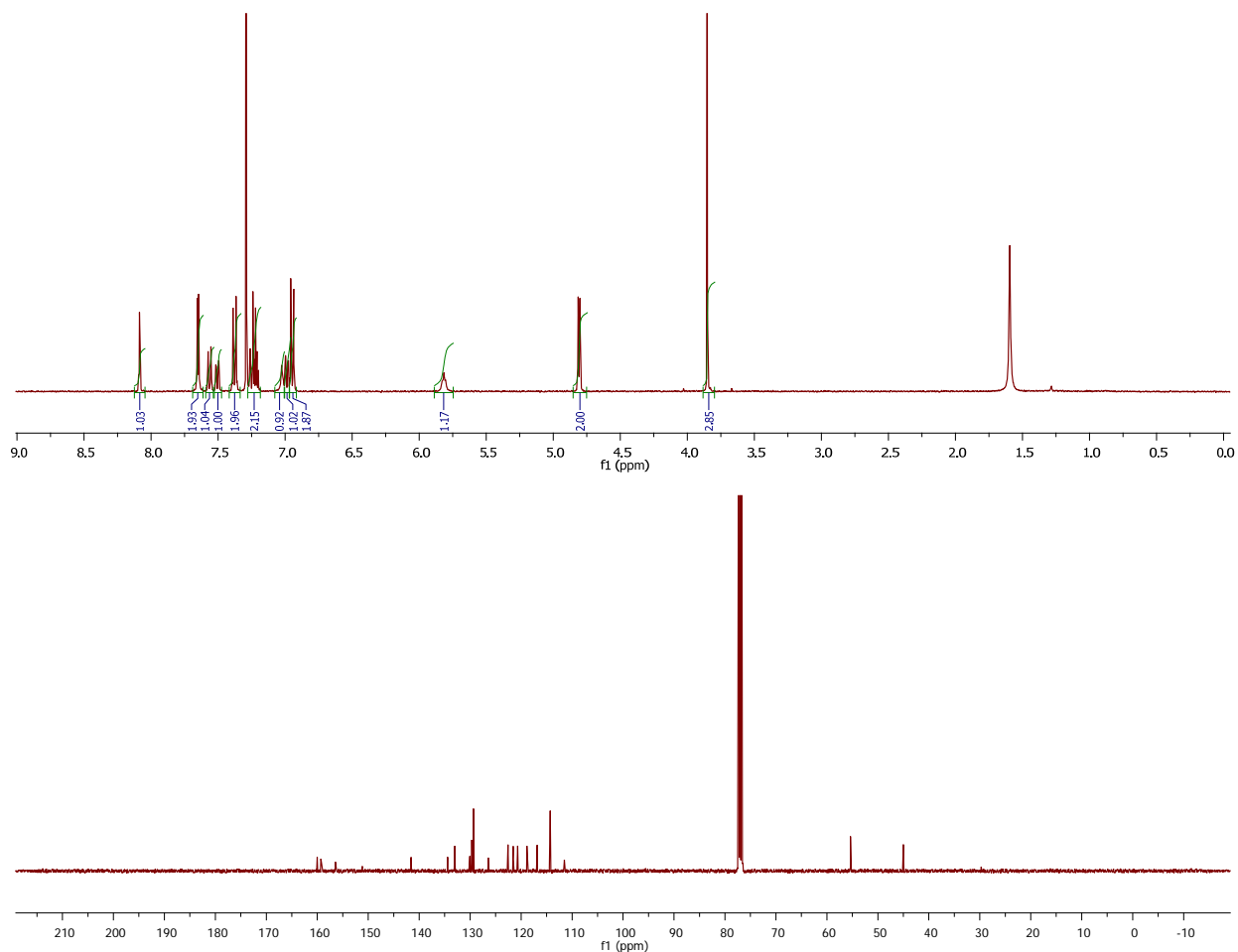
***N*⁴-(4-Bromobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S96).** Yield: 12.5 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 8.04 (t, *J* = 2.0 Hz, 1H), 7.72 – 7.63 (m, 2H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.48 – 7.40 (m, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.27 – 7.20 (m, 2H), 7.05 (s, br. 1H), 7.02 – 6.90 (m, 1H), 5.94 (s, br. 1H), 4.85 (d, *J* = 5.6 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.4, 151.4, 141.5, 137.3, 134.4, 133.2, 131.9, 129.7, 129.4, 126.7, 122.7, 121.6, 121.5, 120.6, 118.9, 116.9, 111.4, 44.6. HRMS (*m/z*): calcd for C₂₁H₁₇BrClN₄ (M+H) 439.0325 and 441.0305; found 441.0296.

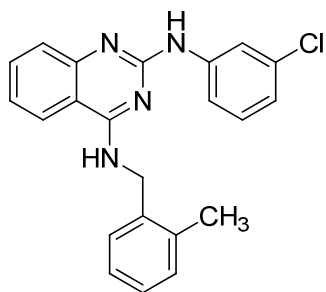




KSC-16-79

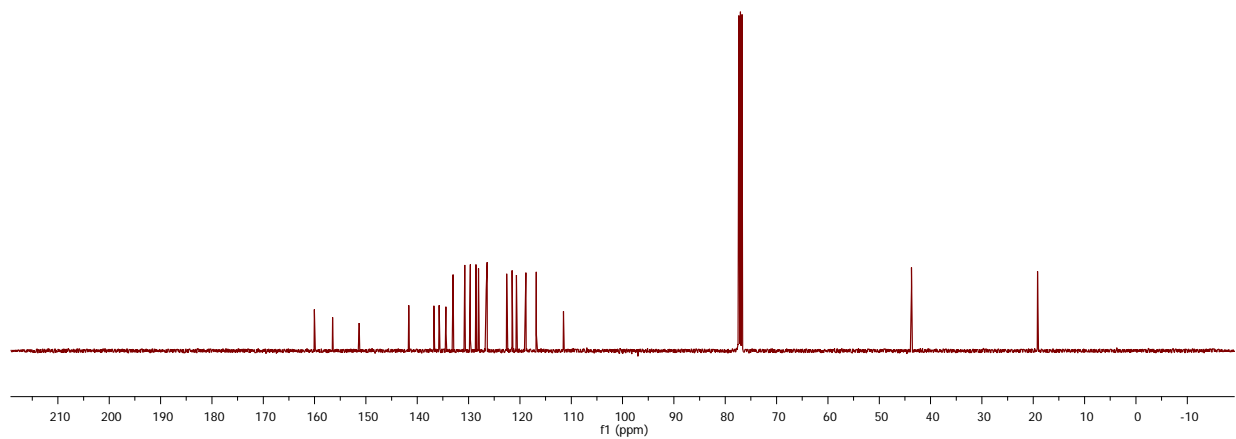
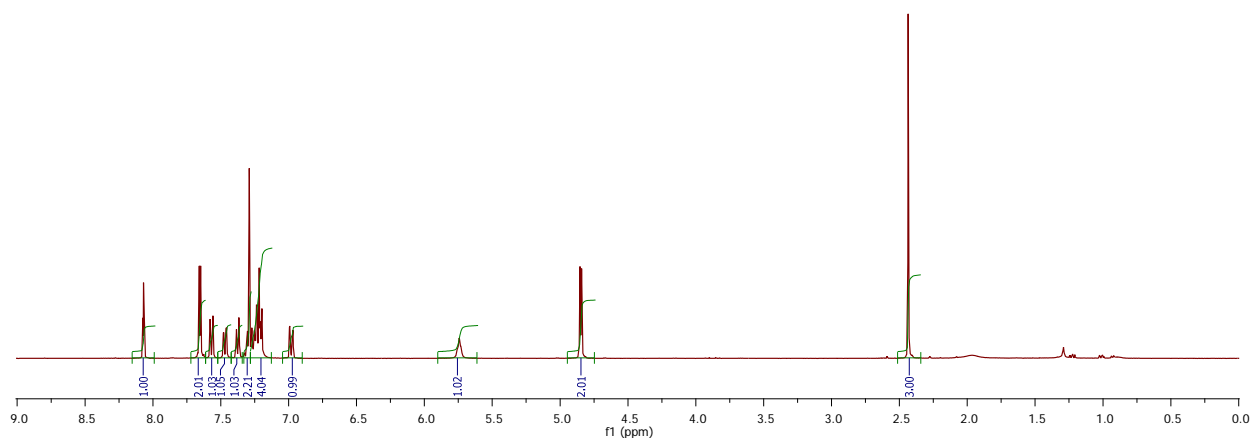
***N*²-(3-Chlorophenyl)-*N*⁴-(4-methoxybenzyl)quinazoline-2,4-diamine (S97).** Yield: 11.3 mg, 87%. ¹H NMR (400 MHz, CDCl₃) δ 8.09 (t, *J* = 2.1 Hz, 1H), 7.65 (d, *J* = 3.5 Hz, 2H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.53 – 7.47 (m, 1H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.23 (dt, *J* = 6.0, 8.2 Hz, 2H), 7.03 (s, br. 1H), 6.99 (dd, *J* = 1.1, 7.9 Hz, 1H), 6.97 – 6.92 (m, 2H), 5.82 (s, br. 1H), 4.81 (d, *J* = 5.2 Hz, 2H), 3.85 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 159.3, 156.4, 151.2, 141.6, 134.4, 133.0, 130.1, 129.7, 129.3, 126.5, 122.6, 121.6, 120.7, 118.9, 116.9, 114.3, 111.5, 55.4, 45.0. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+*H*) 391.1326; found 391.1326.

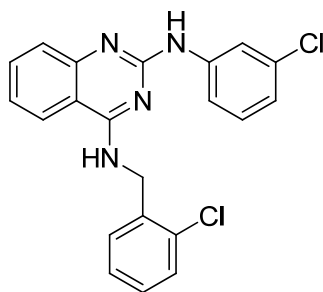




KSC-16-63

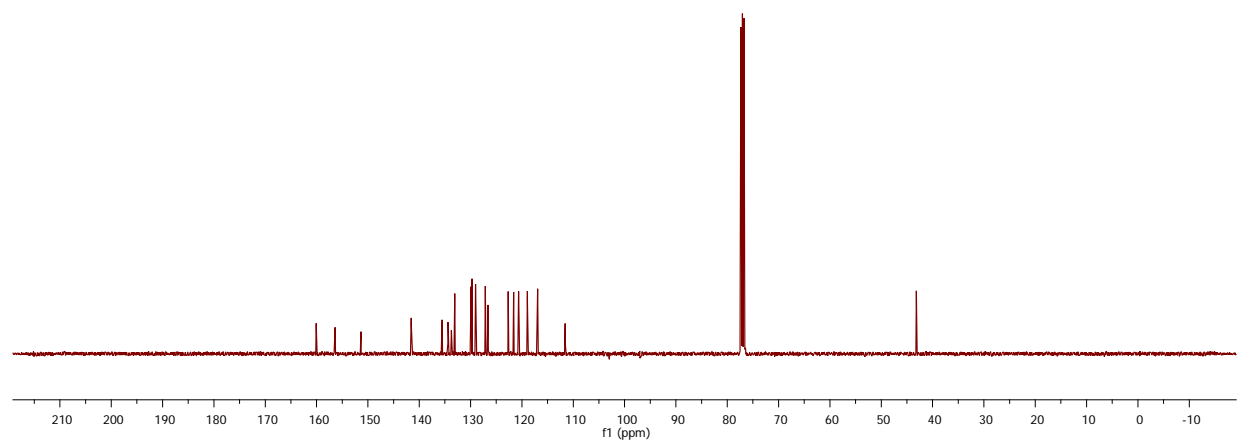
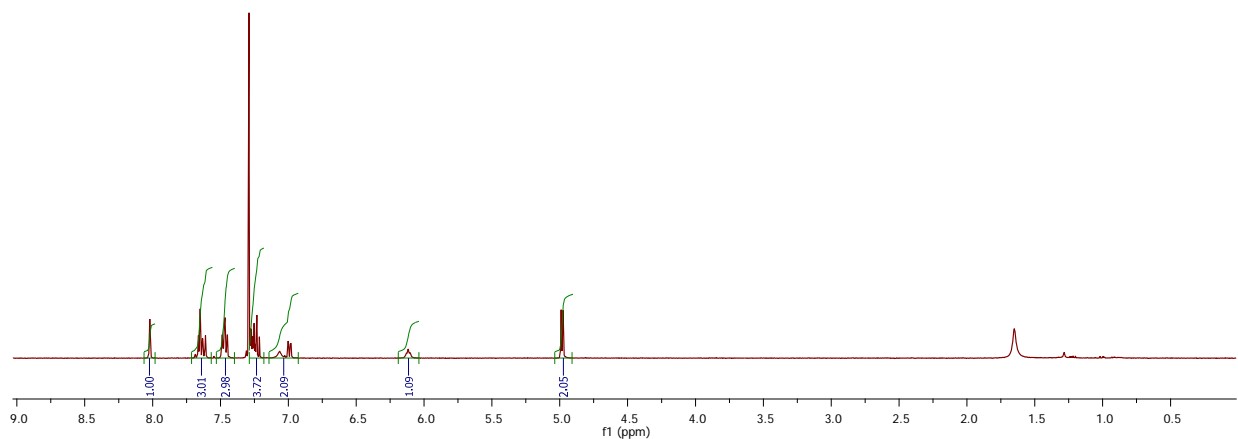
***N*²-(3-Chlorophenyl)-*N*⁴-(2-methylbenzyl)quinazoline-2,4-diamine (S98).** Yield: 12.8 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (t, *J* = 2.0 Hz, 1H), 7.72 – 7.61 (m, 2H), 7.57 (d, *J* = 8.1 Hz, 1H), 7.52 – 7.42 (m, 1H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.32 – 7.30 (m, 2H), 7.28 – 7.13 (m, 4H), 7.04 – 6.90 (m, 1H), 5.74 (s, br. 1H), 4.85 (d, *J* = 5.0 Hz, 2H), 2.44 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.3, 141.7, 136.8, 135.7, 134.4, 133.0, 130.7, 129.7, 128.6, 128.1, 126.6, 126.4, 122.6, 121.5, 120.7, 118.9, 116.8, 111.5, 43.7, 19.2. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+*H*) 375.1376; found 375.1376.

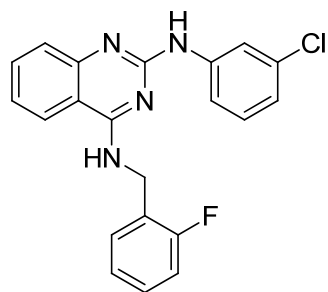




KSC-16-84

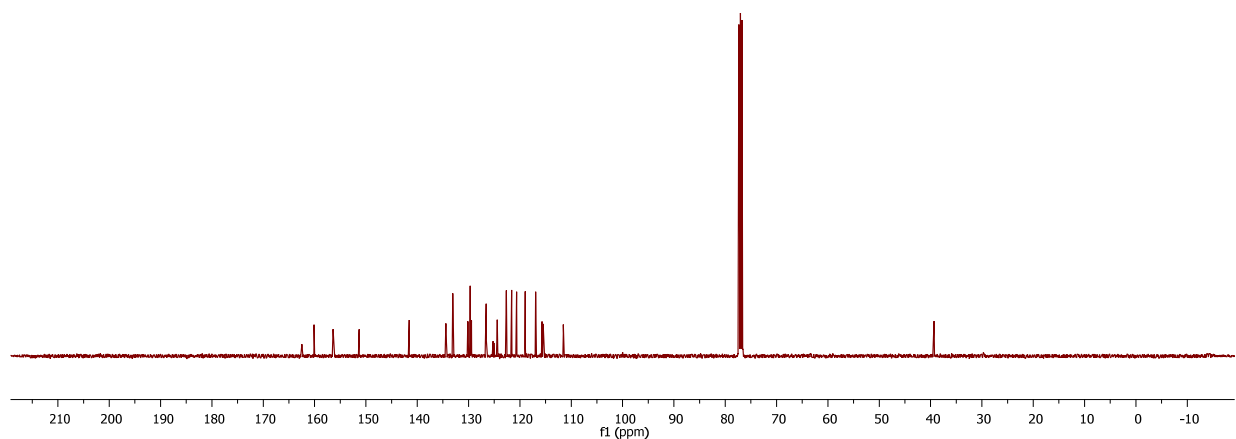
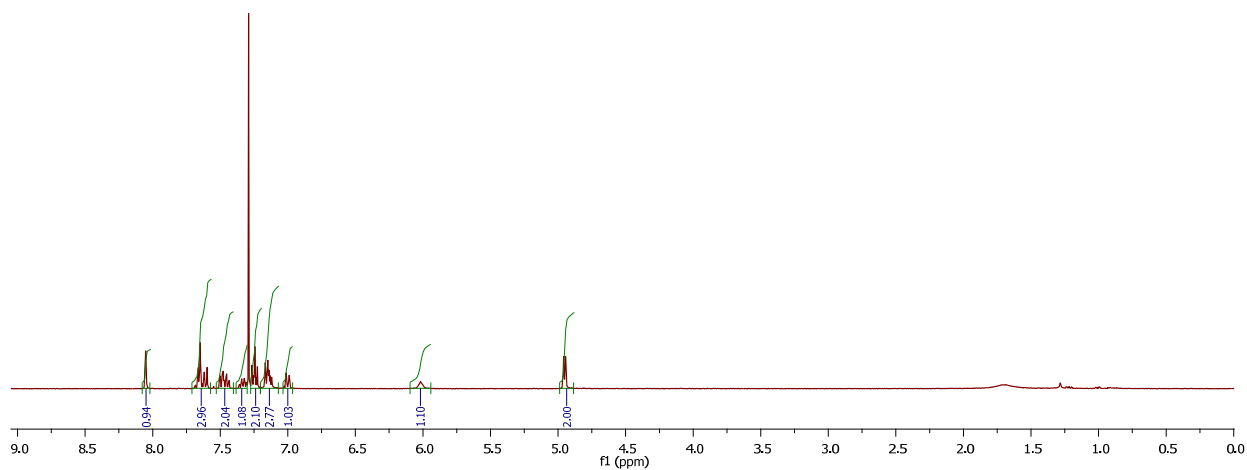
***N*⁴-(2-Chlorobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S99).** Yield: 13.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (t, *J* = 2.1 Hz, 1H), 7.71 – 7.57 (m, 3H), 7.53 – 7.40 (m, 3H), 7.29 – 7.18 (m, 4H), 7.14 – 6.93 (m, 2H), 6.12 (s, br. 1H), 4.98 (d, *J* = 5.8 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.4, 151.4, 141.6, 135.5, 134.4, 133.8, 133.1, 129.9, 129.72, 129.69, 129.0, 127.1, 126.6, 122.7, 121.6, 120.7, 118.9, 116.9, 111.6, 43.2. HRMS (*m/z*): calcd for C₂₁H₁₇Cl₂N₄ (*M*+*H*) 395.0830; found 395.0826.

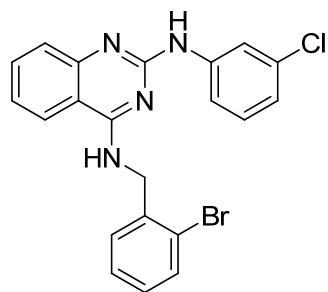




KSC-16-92

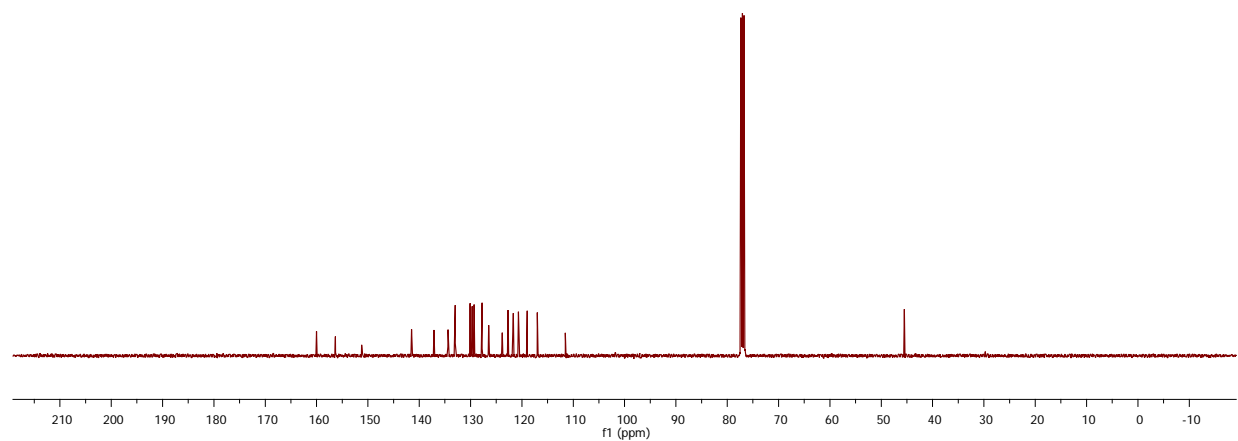
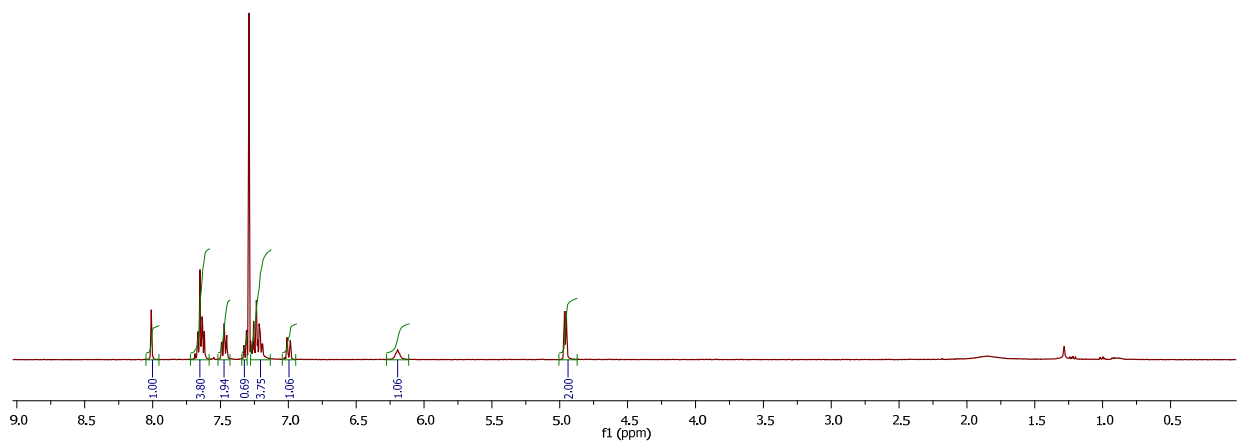
***N*²-(3-Chlorophenyl)-*N*⁴-(2-fluorobenzyl)quinazoline-2,4-diamine (S100).** Yield: 12.4 mg, 94%. ¹H NMR (400 MHz, CDCl₃) δ 8.05 (t, *J* = 2.0 Hz, 1H), 7.71 – 7.57 (m, 3H), 7.53 – 7.40 (m, 2H), 7.38 – 7.30 (m, 1H), 7.28 – 7.20 (m, 2H), 7.20 – 7.07 (m, 3H), 7.04 – 6.96 (m, 1H), 6.02 (s, br. 1H), 4.95 (d, *J* = 5.6 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 162.5, 160.1, 160.0, 156.4, 151.3, 141.6, 134.4, 133.1, 130.2, 130.1, 129.7, 129.5, 129.4, 126.6, 125.2, 125.1, 124.41, 124.38, 122.6, 121.6, 120.7, 119.0, 116.9, 115.7, 115.5, 111.6, 39.4, 39.3. HRMS (*m/z*): calcd for C₂₁H₁₇ClFN₄ (*M*+*H*) 379.1126; found 379.1127.

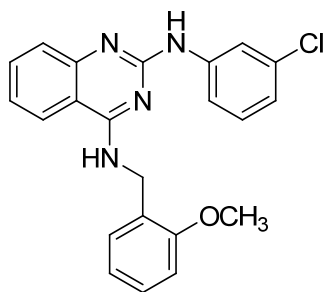




KSC-16-99

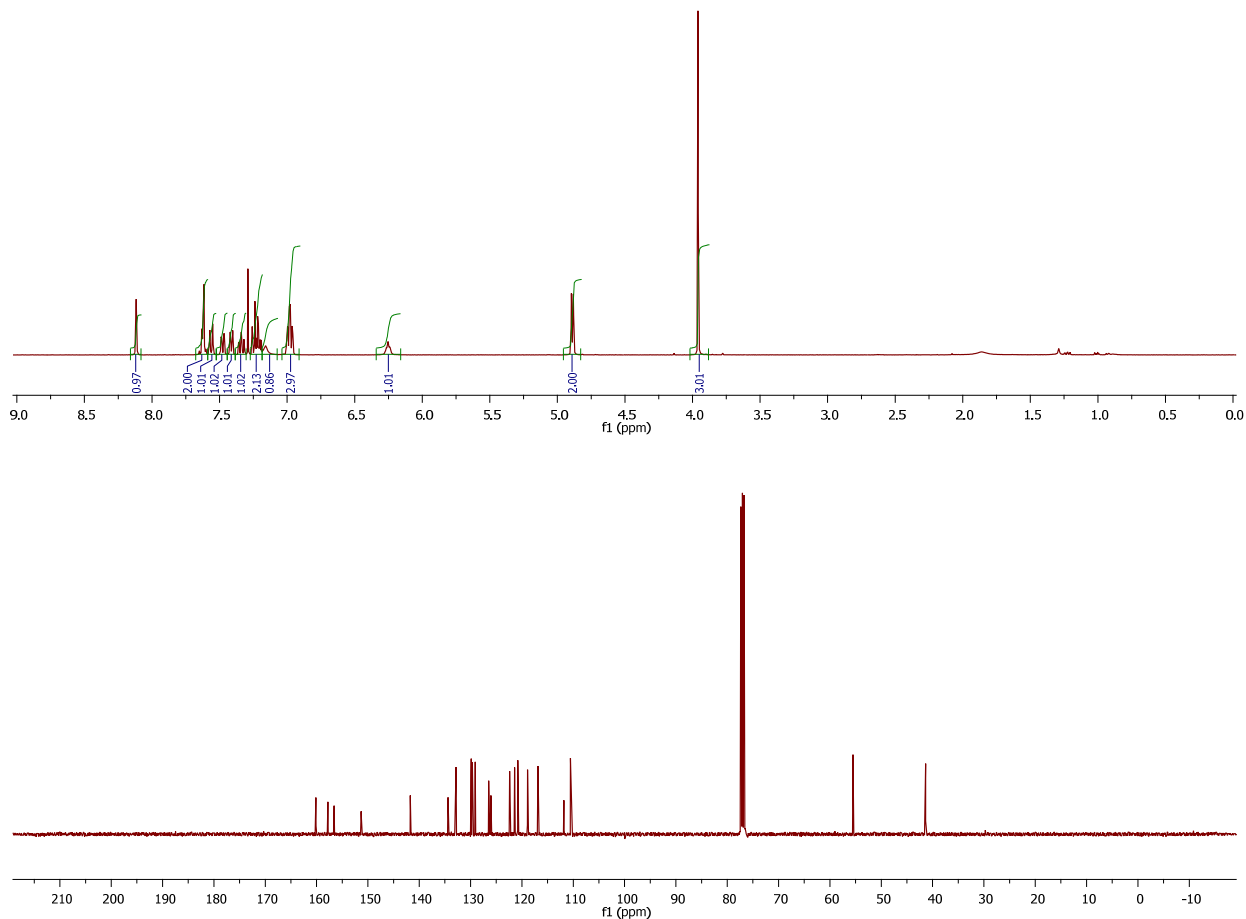
***N*⁴-(2-Bromobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S101).** Yield: 12.3 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.01 (t, *J* = 2.0 Hz, 1H), 7.67 – 7.62 (m, 4H), 7.49 – 7.45 (m, 2H), 7.34 – 7.30 (m, 1H), 7.28 – 7.13 (m, 4H), 7.04 – 6.95 (m, 1H), 6.19 (s, br. 1H), 4.96 (d, *J* = 5.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 156.3, 151.2, 141.5, 137.1, 134.4, 133.1, 133.0, 130.1, 129.7, 129.3, 127.8, 126.5, 123.8, 122.7, 121.7, 120.7, 119.0, 117.0, 111.5, 45.5. HRMS (*m/z*): calcd for C₂₁H₁₇BrClN₄ (*M*+*H*) 439.0325 and 441.0305; found 441.0298.

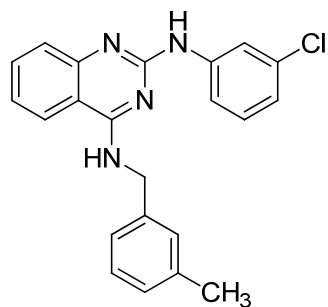




KSC-16-75

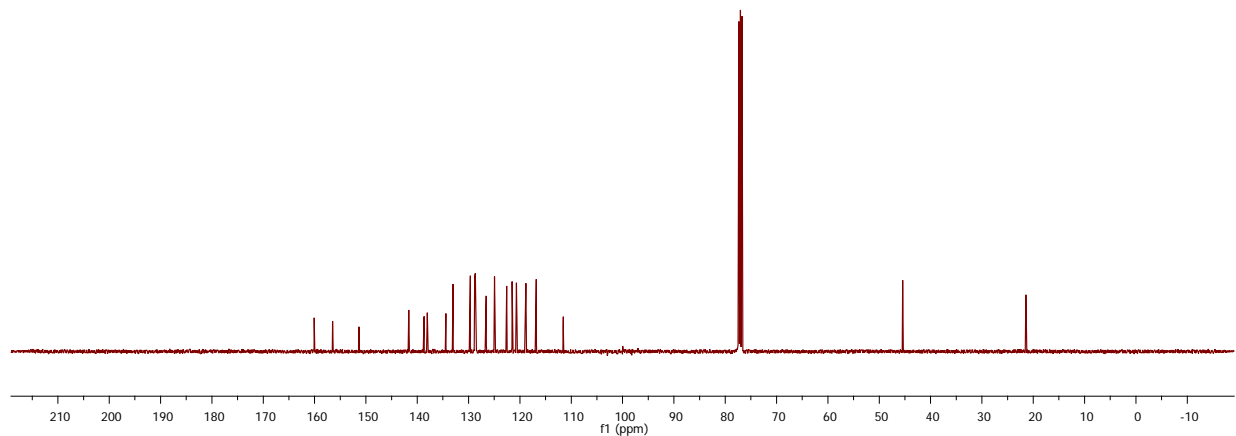
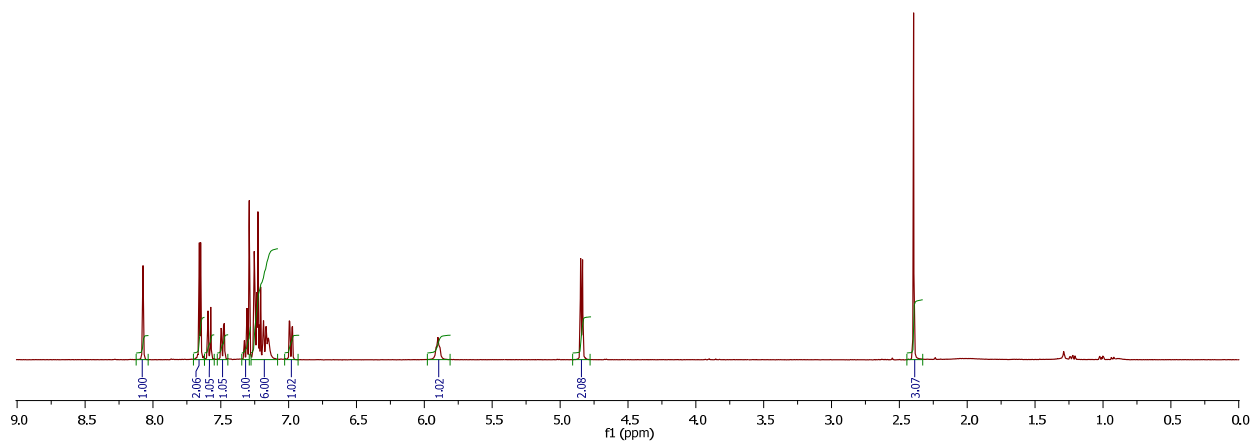
***N*²-(3-Chlorophenyl)-*N*⁴-(2-methoxybenzyl)quinazoline-2,4-diamine (S102).** Yield: 13.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.12 (t, *J* = 2.1 Hz, 1H), 7.68 – 7.59 (m, 2H), 7.56 (d, *J* = 8.2 Hz, 1H), 7.48 (ddd, *J* = 0.9, 2.1, 8.2 Hz, 1H), 7.41 (dd, *J* = 1.7, 7.6 Hz, 1H), 7.38 – 7.30 (m, 1H), 7.27 – 7.18 (m, 2H), 7.16 (s, br. 1H), 7.04 – 6.91 (m, 3H), 6.25 (s, br. 1H), 4.89 (d, *J* = 5.6 Hz, 2H), 3.96 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 157.8, 156.6, 151.3, 141.8, 134.4, 132.8, 129.9, 129.6, 129.1, 126.5, 126.1, 122.4, 121.4, 120.8, 120.7, 118.9, 116.9, 111.8, 110.5, 55.5, 41.4. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+*H*) 391.1326; found 391.1327.

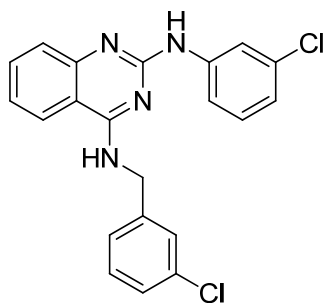




KSC-16-66

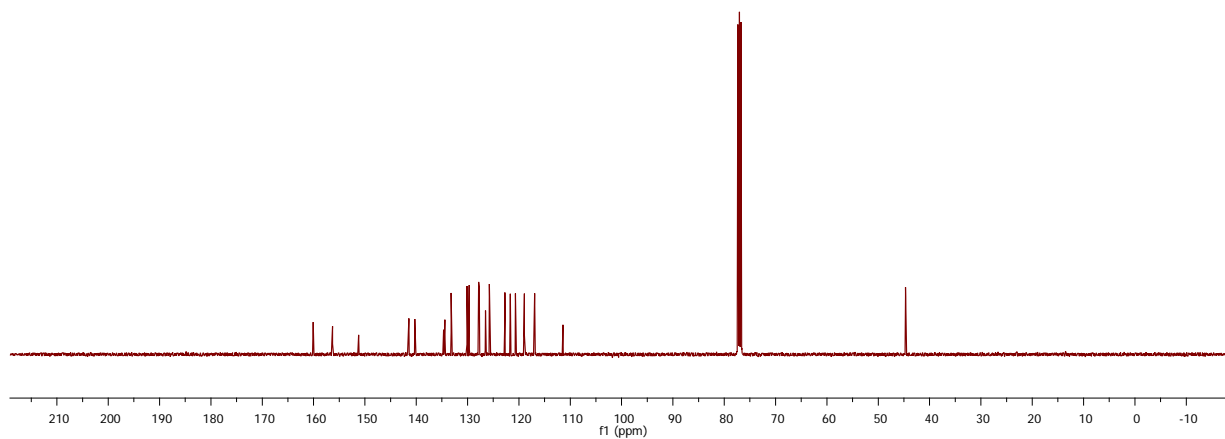
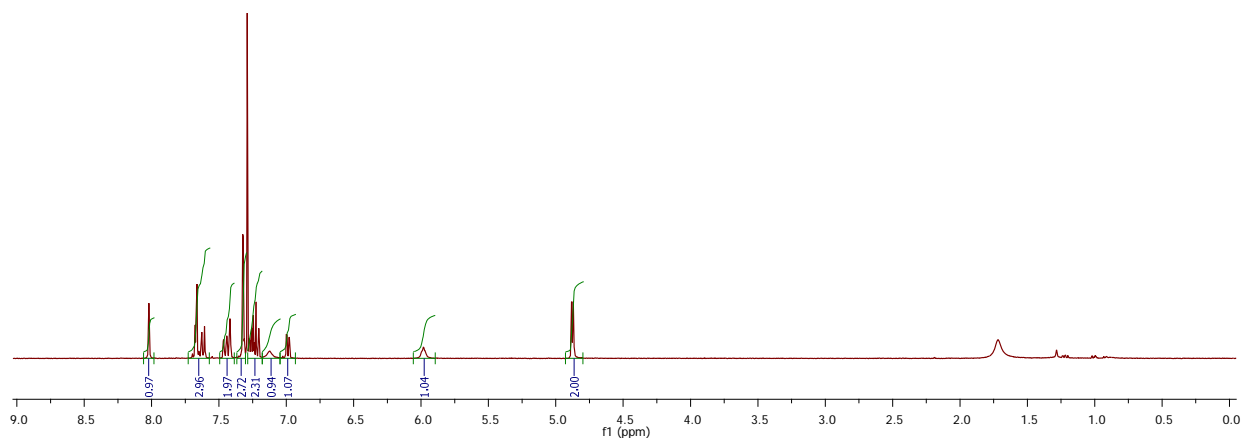
***N*²-(3-Chlorophenyl)-*N*⁴-(3-methylbenzyl)quinazoline-2,4-diamine (S103).** Yield: 13.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.07 (t, *J* = 2.1 Hz, 1H), 7.65 (d, *J* = 3.5 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 1H), 7.49 (ddd, *J* = 0.9, 2.1 Hz, 8.2, 1H), 7.34 – 7.29 (m, 1H), 7.28 – 7.08 (m, 6H), 6.98 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H), 5.90 (s, br. 1H), 4.84 (d, *J* = 5.2 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.5, 151.3, 141.6, 138.7, 138.0, 134.4, 133.0, 129.7, 128.8, 128.7, 128.5, 126.6, 125.0, 122.6, 121.5, 120.7, 118.8, 116.8, 111.6, 45.4, 21.4. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (M+H) 375.1376; found 375.1379.

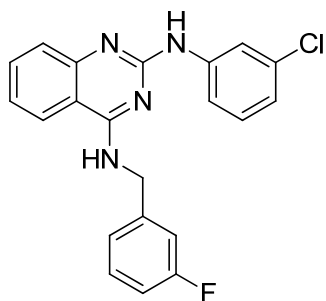




KSC-16-87

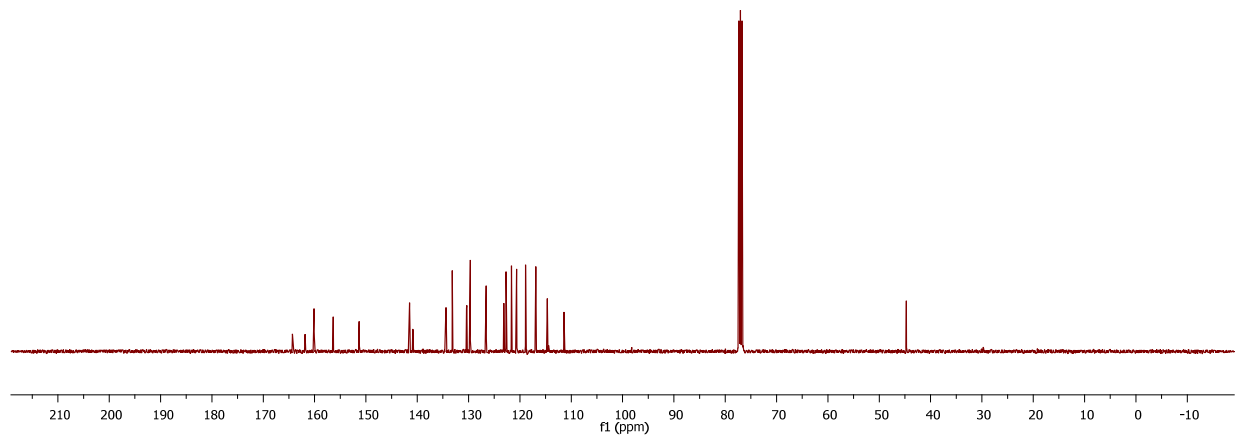
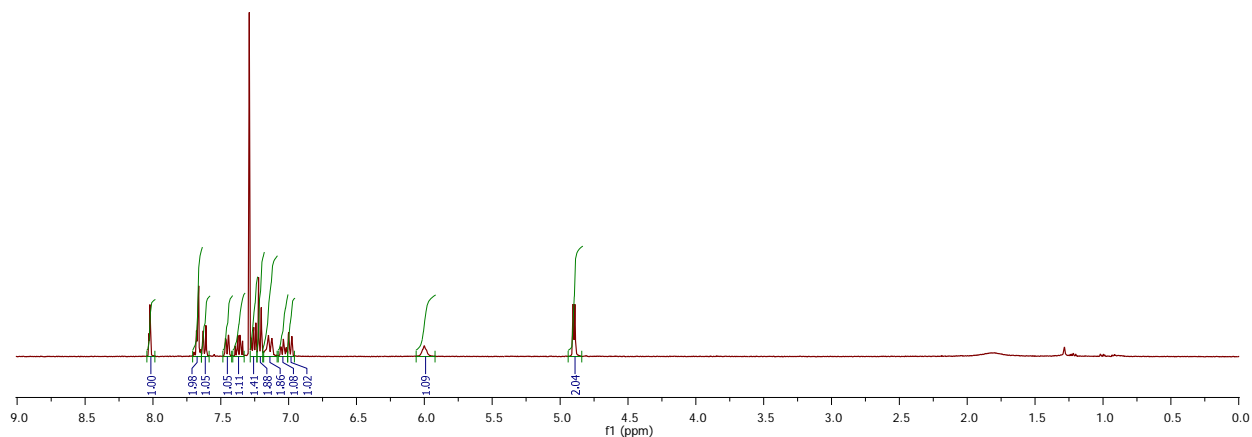
***N*⁴-(3-Chlorobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S104).** Yield: 13.0 mg 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (t, *J* = 2.0 Hz, 1H), 7.73 – 7.57 (m, 3H), 7.49 – 7.39 (m, 2H), 7.33 – 7.32 (m, 3H), 7.29 – 7.18 (m, 2H), 7.12 (s, br. 1H), 7.05 – 6.93 (m, 1H), 5.98 (s, br. 1H), 4.88 (d, *J* = 5.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.3, 151.2, 141.4, 140.3, 134.7, 134.4, 133.2, 130.1, 129.7, 127.8, 127.7, 126.5, 125.8, 122.7, 121.7, 120.7, 119.0, 117.0, 111.4, 44.7. HRMS (*m/z*): calcd for C₂₁H₁₇Cl₂N₄ (*M*+*H*) 395.0830; found 395.0826.

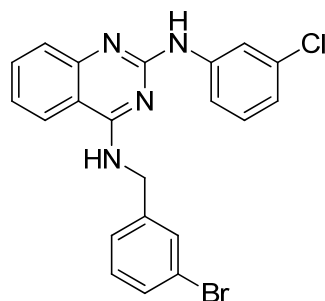




KSC-16-95

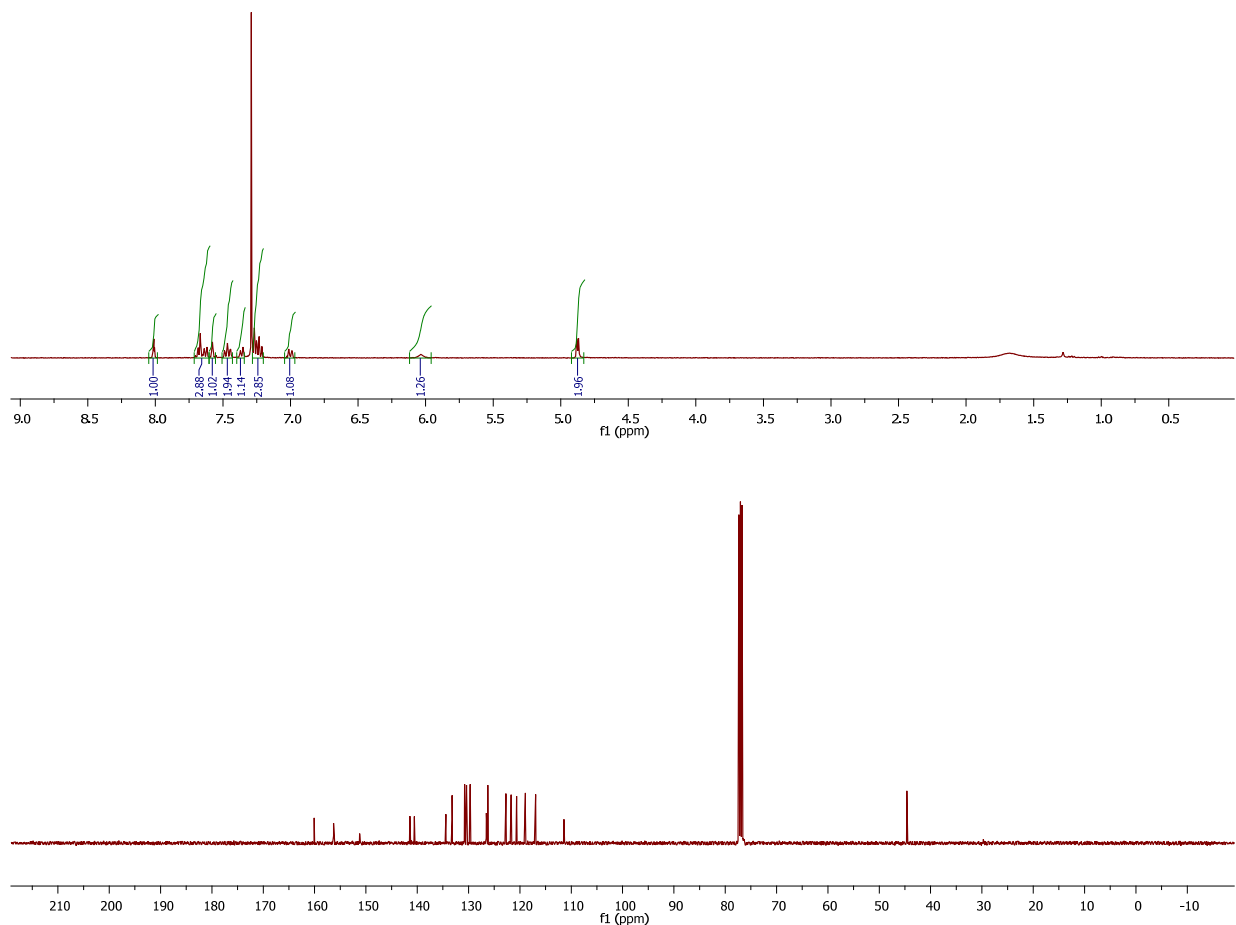
***N*²-(3-Chlorophenyl)-*N*⁴-(3-fluorobenzyl)quinazoline-2,4-diamine (S105).** Yield: 13.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (t, *J* = 2.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.62 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.41 – 7.33 (m, 1H), 7.28 – 7.23 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.15 – 7.12 (m, 2H), 7.04 (t, *J* = 8.2 Hz, 1H), 6.99 (dd, *J* = 1.1, 7.9 Hz, 1H), 6.00 (s, br. 1H), 4.90 (d, *J* = 5.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.3, 161.9, 160.1, 156.4, 151.3, 141.5, 140.9, 140.8, 134.4, 133.2, 130.4, 130.3, 123.0, 126.6, 123.2, 123.1, 122.7, 121.6, 120.6, 118.9, 116.9, 114.66, 114.65, 114.5, 114.4, 111.4, 44.73, 44.71. HRMS (*m/z*): calcd for C₂₁H₁₇ClFN₄ (M+H) 379.1126; found 379.1125.

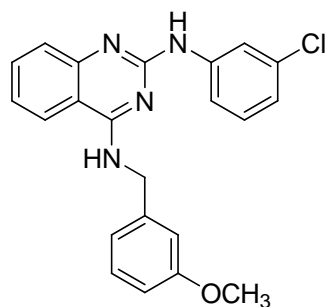




KSC-16-100

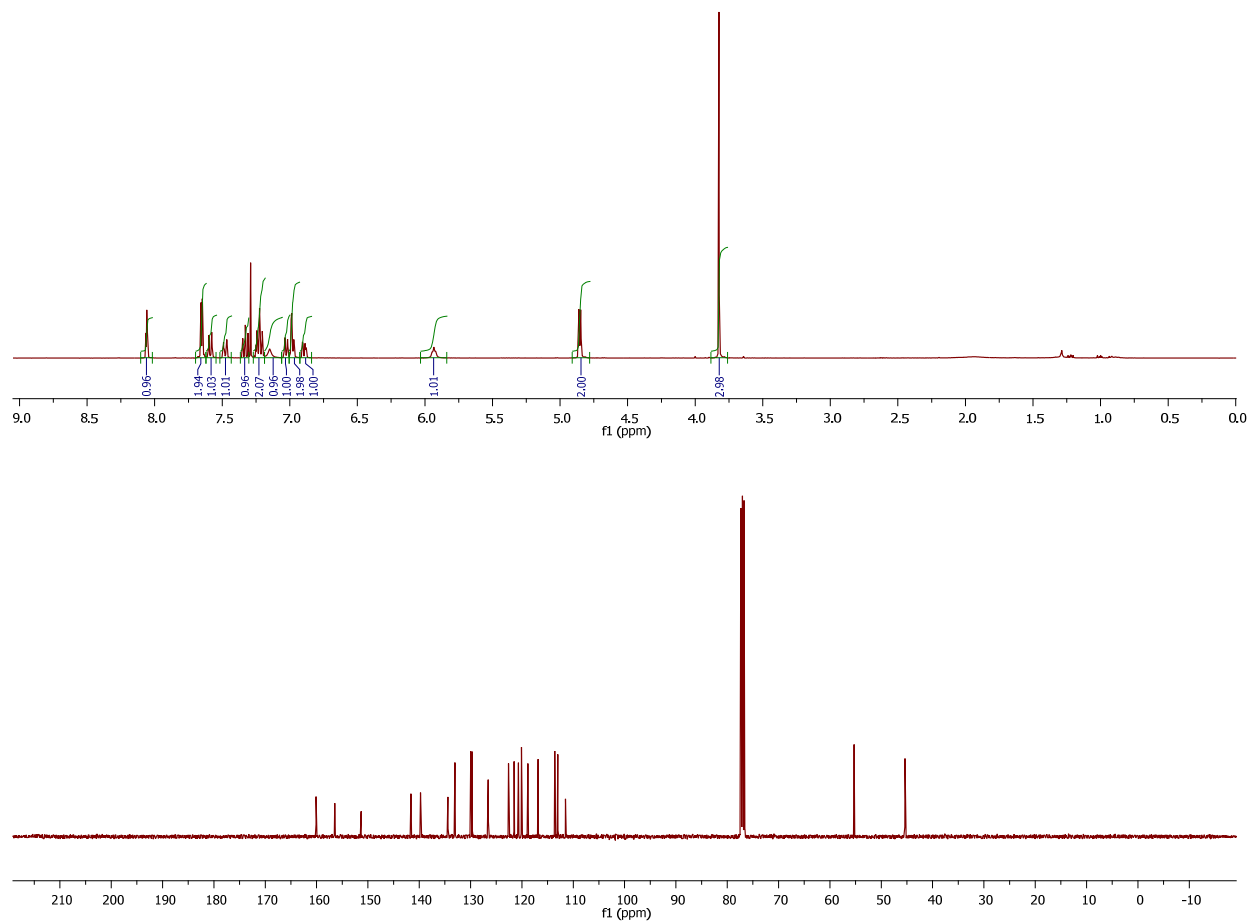
***N*⁴-(3-Bromobenzyl)-*N*²-(3-chlorophenyl)quinazoline-2,4-diamine (S106).** Yield: 12.3 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 8.01 (s, 1H), 7.68 – 7.62 (m, 3H), 7.58 (s, 1H), 7.47 (t, *J* = 9.1 Hz, 2H), 7.36 (d, *J* = 7.7 Hz, 1H), 7.28 – 7.20 (m, 3H), 7.00 (d, *J* = 9.0 Hz, 1H), 6.04 (s, br. 1H), 4.87 (d, *J* = 5.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 156.3, 151.2, 141.4, 140.6, 134.4, 133.2, 130.8, 130.7, 130.4, 129.7, 126.5, 126.2, 122.9, 122.7, 121.7, 120.7, 118.9, 116.9, 111.4, 44.6. HRMS (*m/z*): calcd for C₂₁H₁₇BrClN₄ (*M*+H) 439.0325 and 441.0305; found 441.0299.

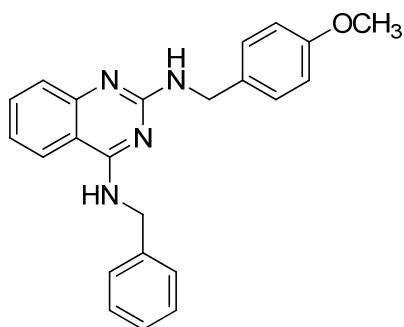




KSC-16-78

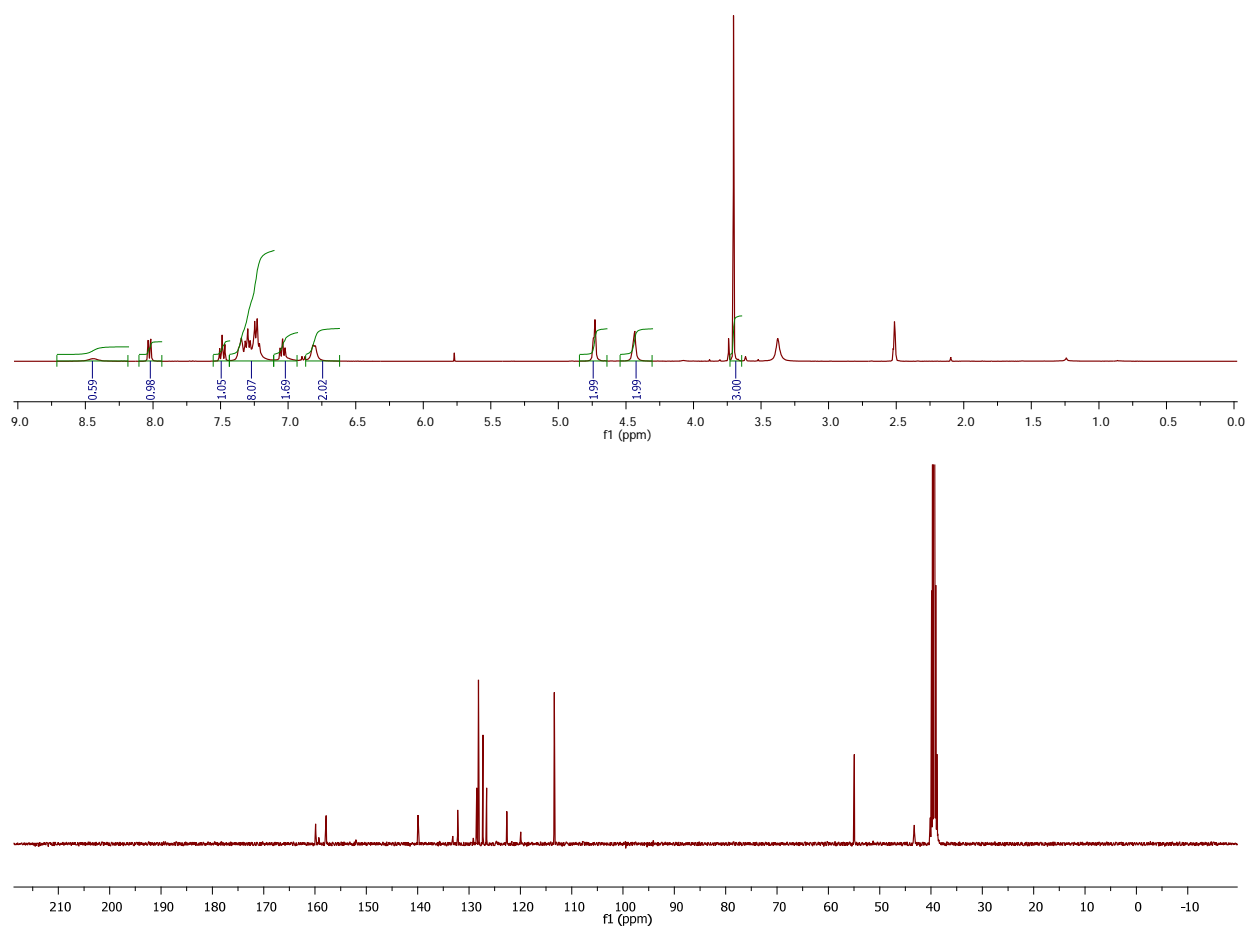
***N*²-(3-Chlorophenyl)-*N*⁴-(3-methoxybenzyl)quinazoline-2,4-diamine (S107).** Yield: 13.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 8.06 (t, *J* = 2.1 Hz, 1H), 7.70 – 7.62 (m, 2H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.48 (ddd, *J* = 0.9, 2.1, 8.2 Hz, 1H), 7.37 – 7.30 (m, 1H), 7.24 – 7.20 (m, 2H), 7.15 (s, br. 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 7.00 – 6.93 (m, 2H), 6.89 (dd, *J* = 1.9, 8.2 Hz, 1H), 5.93 (s, br. 1H), 4.85 (d, *J* = 5.3 Hz, 2H), 3.82 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 160.0, 156.5, 151.3, 141.6, 139.8, 134.4, 133.0, 130.0, 129.7, 126.6, 122.6, 121.5, 120.7, 120.0, 118.8, 116.8, 113.6, 113.0, 111.5, 55.3, 45.4. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+*H*) 391.1326; found 391.1326.

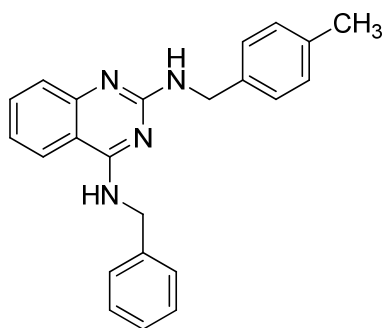




KSC-16-2

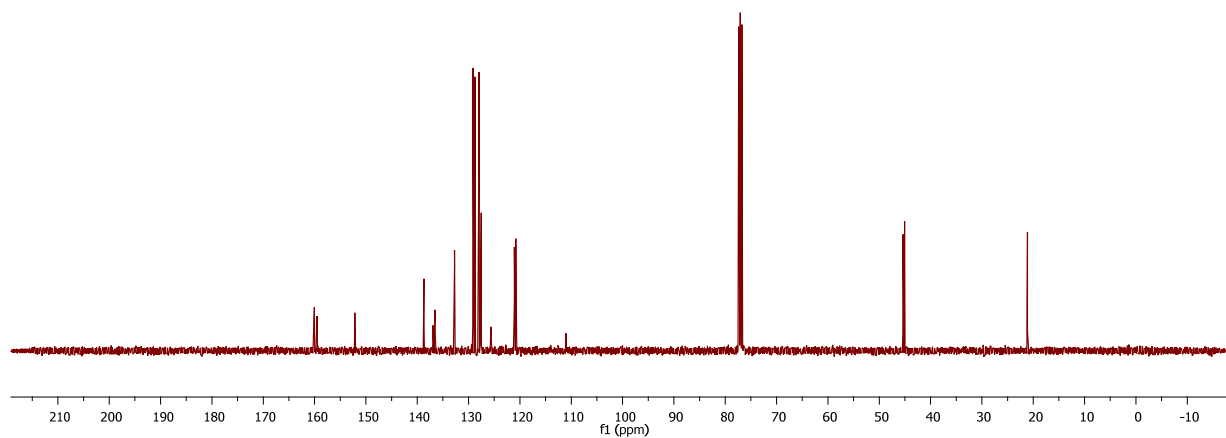
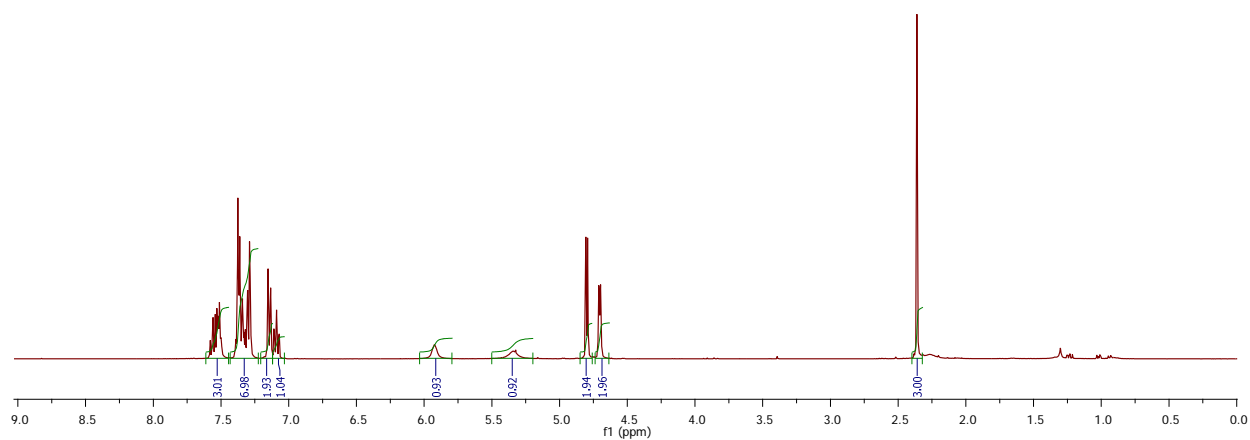
***N*⁴-Benzyl-*N*²-(4-methoxybenzyl)quinazoline-2,4-diamine (S108 or 13).** Yield: 22.0 mg, 80%. ¹H NMR (400 MHz, DMSO) δ 8.44 (s, 1H), 8.03 (d, *J* = 7.3 Hz, 1H), 7.55 – 7.43 (m, 1H), 7.43 – 7.11 (m, 8H), 7.04 (t, *J* = 7.1 Hz, 2H), 6.82 (s, br. 2H), 4.74 (d, *J* = 4.7 Hz, 2H), 4.43 (s, br. 2H), 3.70 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 159.9, 159.8, 159.3, 157.8, 139.9, 133.2, 132.2, 129.2, 128.5, 128.2, 127.3, 126.6, 122.7, 119.9, 113.5, 113.4, 54.9, 43.4, 43.3. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (*M*+H) 371.1872; found 371.1868.

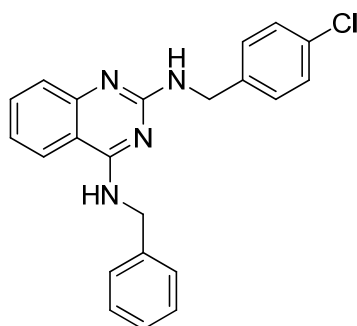




KSC-1-300

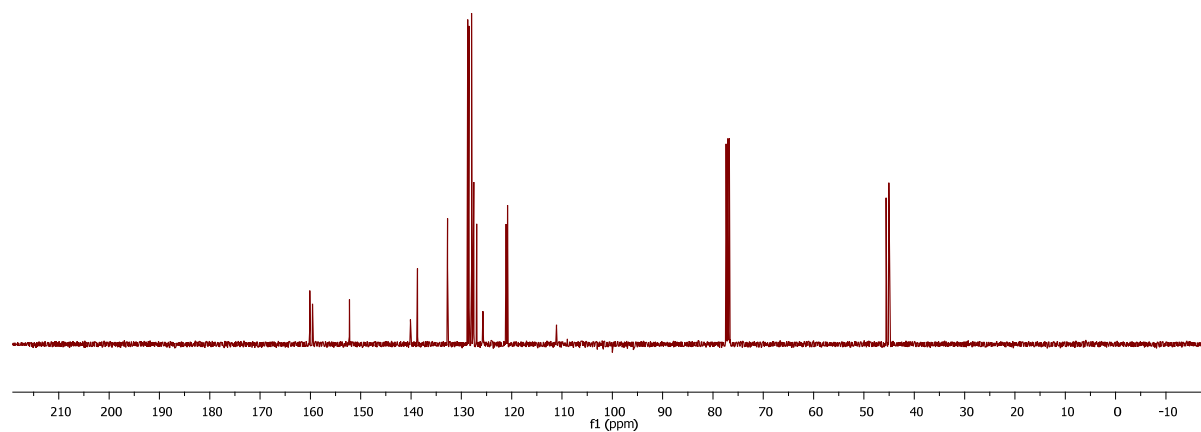
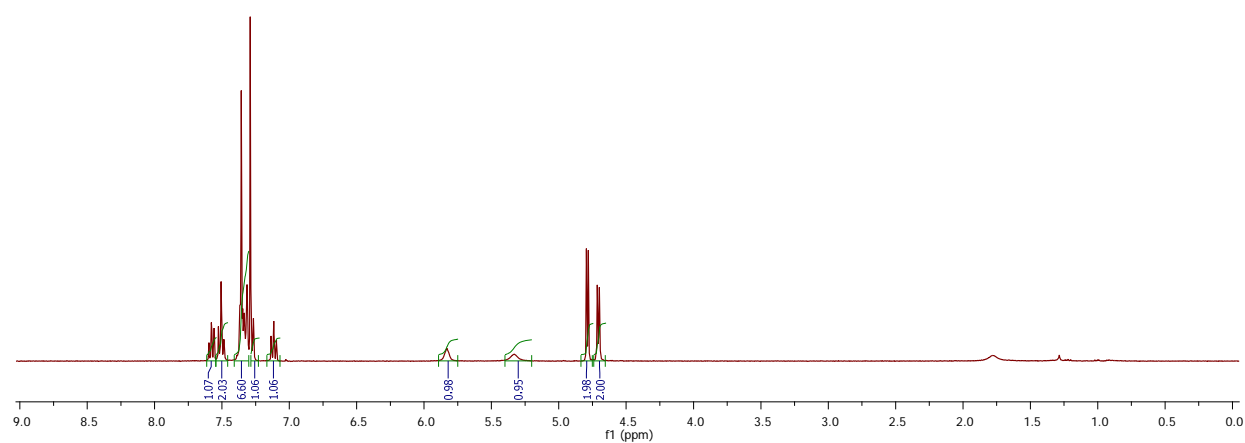
***N*⁴-Benzyl-*N*²-(4-methylbenzyl)quinazoline-2,4-diamine (S109 or 45).** Yield: 24.0 mg, 91%. ¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.44 (m, 3H), 7.43 – 7.22 (m, 7H), 7.14 (d, *J* = 7.8 Hz, 2H), 7.12 – 7.03 (m, 1H), 5.92 (s, br. 1H), 5.32 (s, br. 1H), 4.80 (d, *J* = 5.4 Hz, 2H), 4.70 (d, *J* = 5.1 Hz, 2H), 2.36 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.5, 152.2, 138.7, 137.0, 136.6, 132.7, 129.2, 128.7, 128.0, 127.6, 127.5, 125.6, 121.1, 120.8, 111.0, 45.4, 45.1, 21.1. HRMS (*m/z*): calcd for C₂₃H₂₃N₄ (*M*+*H*) 355.1923; found 355.1924.

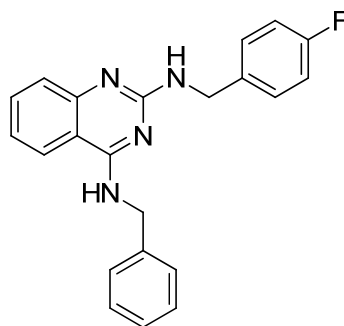




KSC-16-33

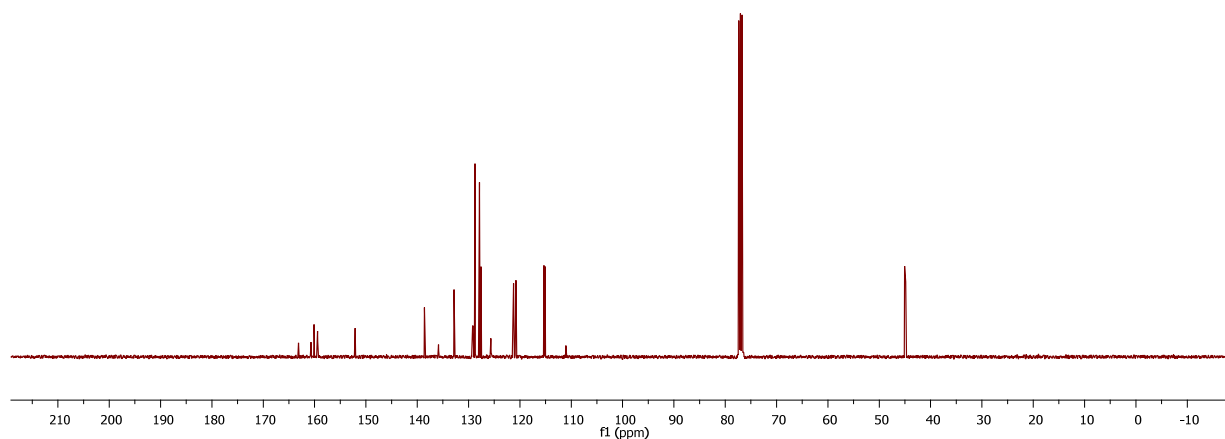
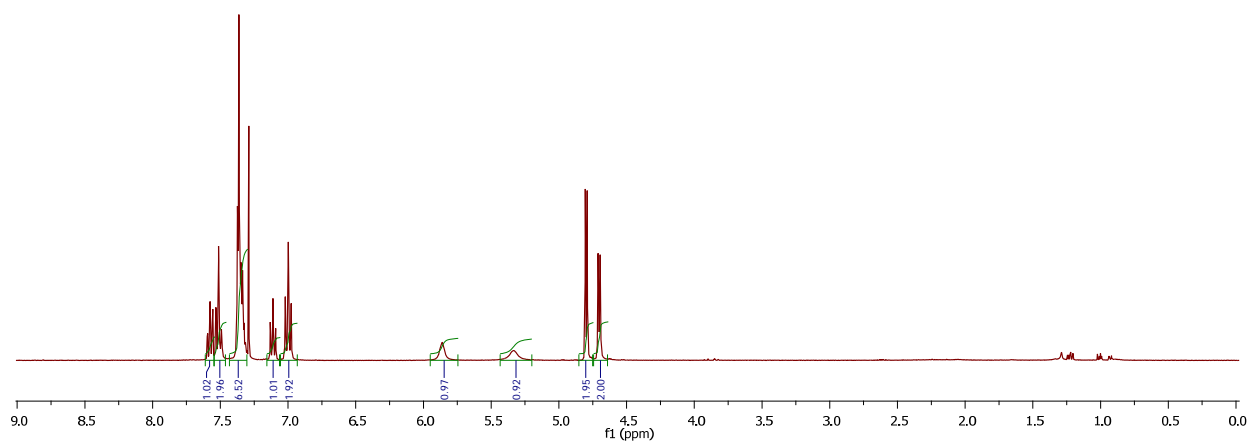
***N*⁴-Benzyl-*N*²-(4-chlorobenzyl)quinazoline-2,4-diamine (S110).** Yield: 27.0 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.55 (m, 1H), 7.51 (t, *J* = 8.1, 2H), 7.41 – 7.30 (m, 7H), 7.29 – 7.277 (m, 2H), 7.14 – 7.10 (m, 1H), 5.83 (s, br. 1H), 5.33 (s, br. 1H), 4.79 (d, *J* = 5.5 Hz, 2H), 4.71 (d, *J* = 6.0 Hz, 2H). HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (M+H) 375.1376; found 375.1369.

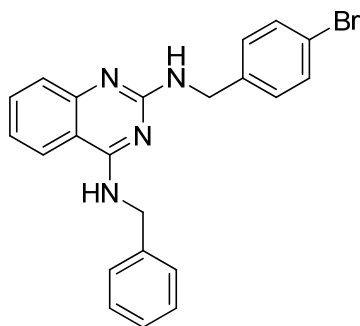




KSC-16-38

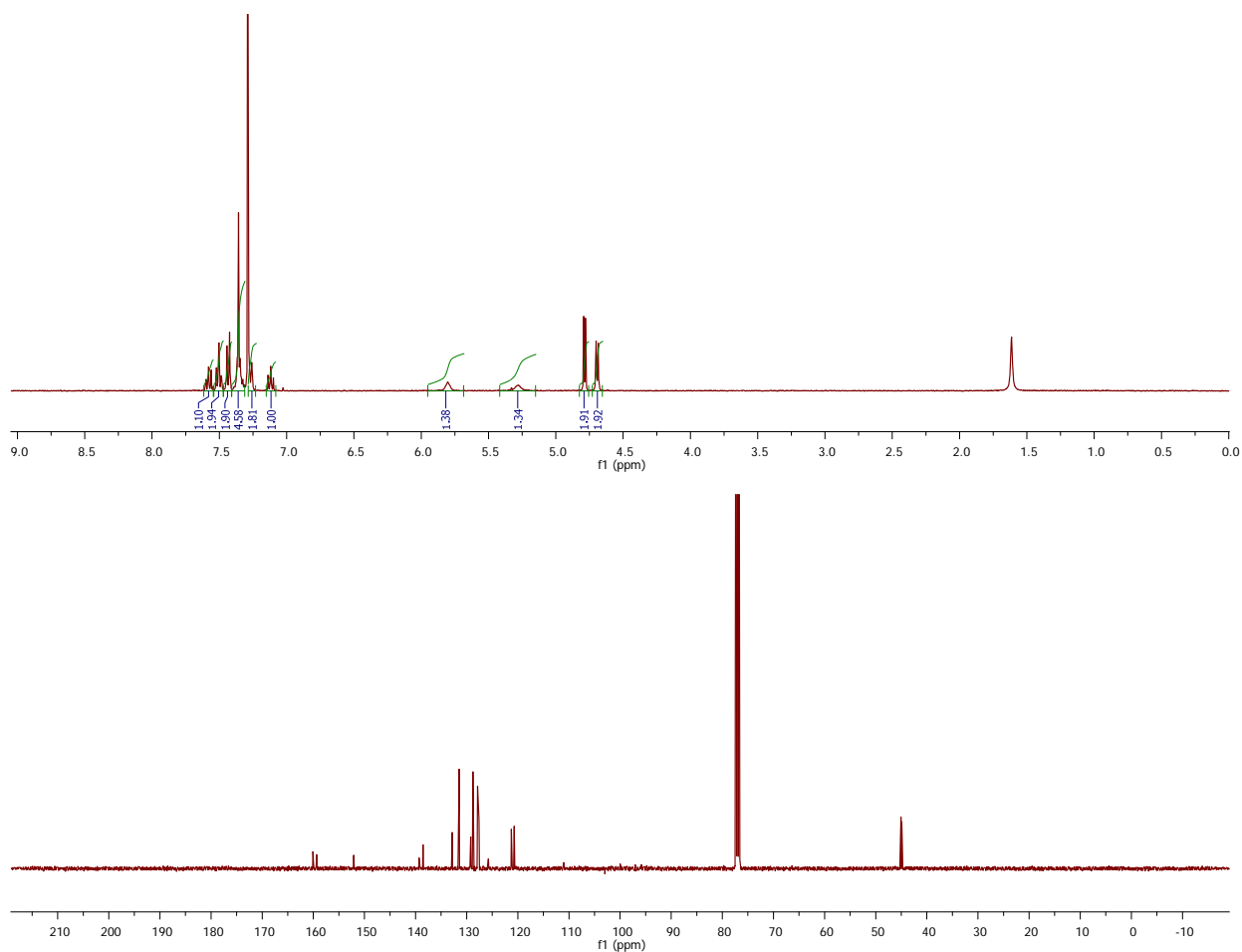
***N*⁴-Benzyl-*N*²-(4-fluorobenzyl)quinazoline-2,4-diamine (S111).** Yield: 26.5 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.51 (t, *J* = 8.3 Hz, 2H), 7.43 – 7.30 (m, 7H), 7.11 (ddd, *J* = 1.3, 6.9, 8.2 Hz, 1H), 7.00 (t, *J* = 8.7 Hz, 2H), 5.86 (s, br. 1H), 5.33 (s, br. 1H), 4.80 (d, *J* = 5.5 Hz, 2H), 4.70 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 163.1, 160.7, 160.1, 159.4, 152.1, 138.6, 135.9, 132.8, 129.2, 129.1, 128.8, 127.9, 127.6, 125.8, 121.2, 120.9, 115.3, 115.1, 111.0, 45.1, 44.8. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1672.

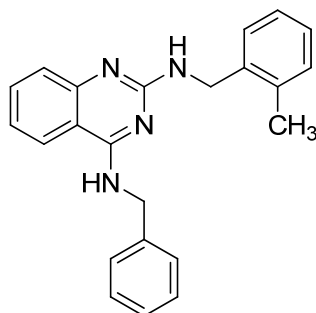




KSC-16-42

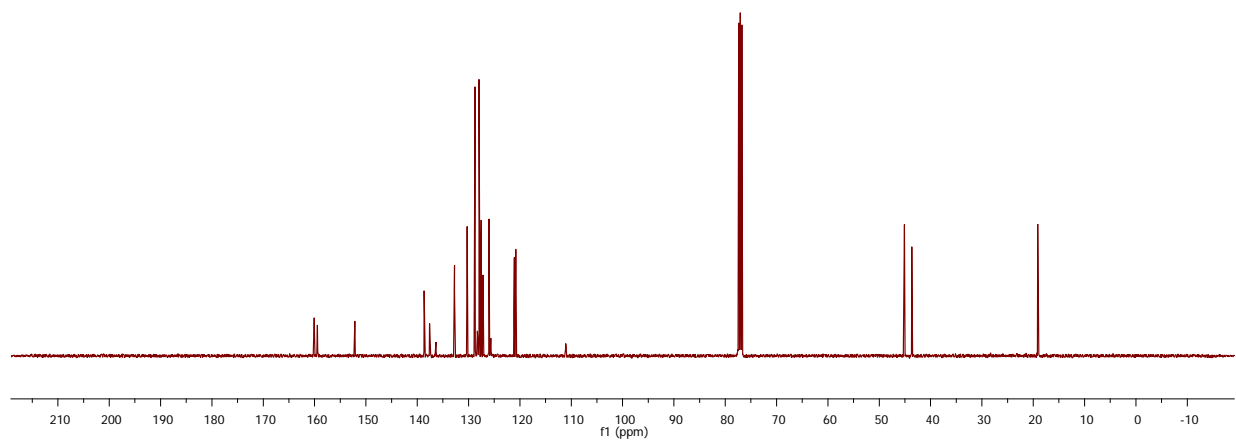
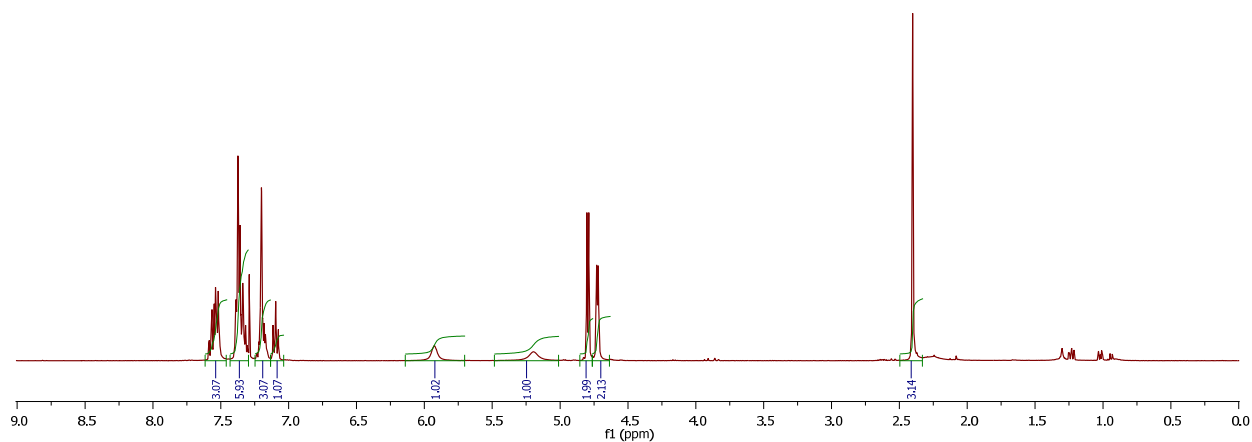
***N*⁴-Benzyl-*N*²-(4-bromobenzyl)quinazoline-2,4-diamine (S112).** Yield: 31.0 mg, 100%. ¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.54 (m, 1H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.37 – 7.33 (m, 5H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.12 (t, *J* = 8.1 Hz, 1H), 5.80 (s, br. 1H), 5.28 (s, br. 1H), 4.79 (d, *J* = 5.5 Hz, 2H), 4.69 (d, *J* = 6.1 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.1, 139.3, 138.5, 132.8, 131.5, 129.2, 128.8, 127.9, 127.6, 125.8, 121.3, 120.7, 120.7, 111.1, 45.1, 44.9. HRMS (*m/z*): calcd for C₂₂H₂₀BrN₄ (*M*+*H*) 419.0871 and 421.0851; found 421.0846.

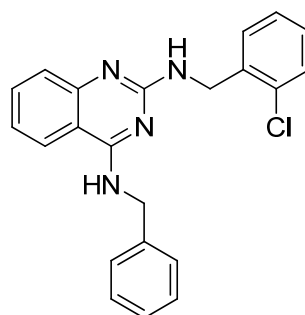




KSC-16-8

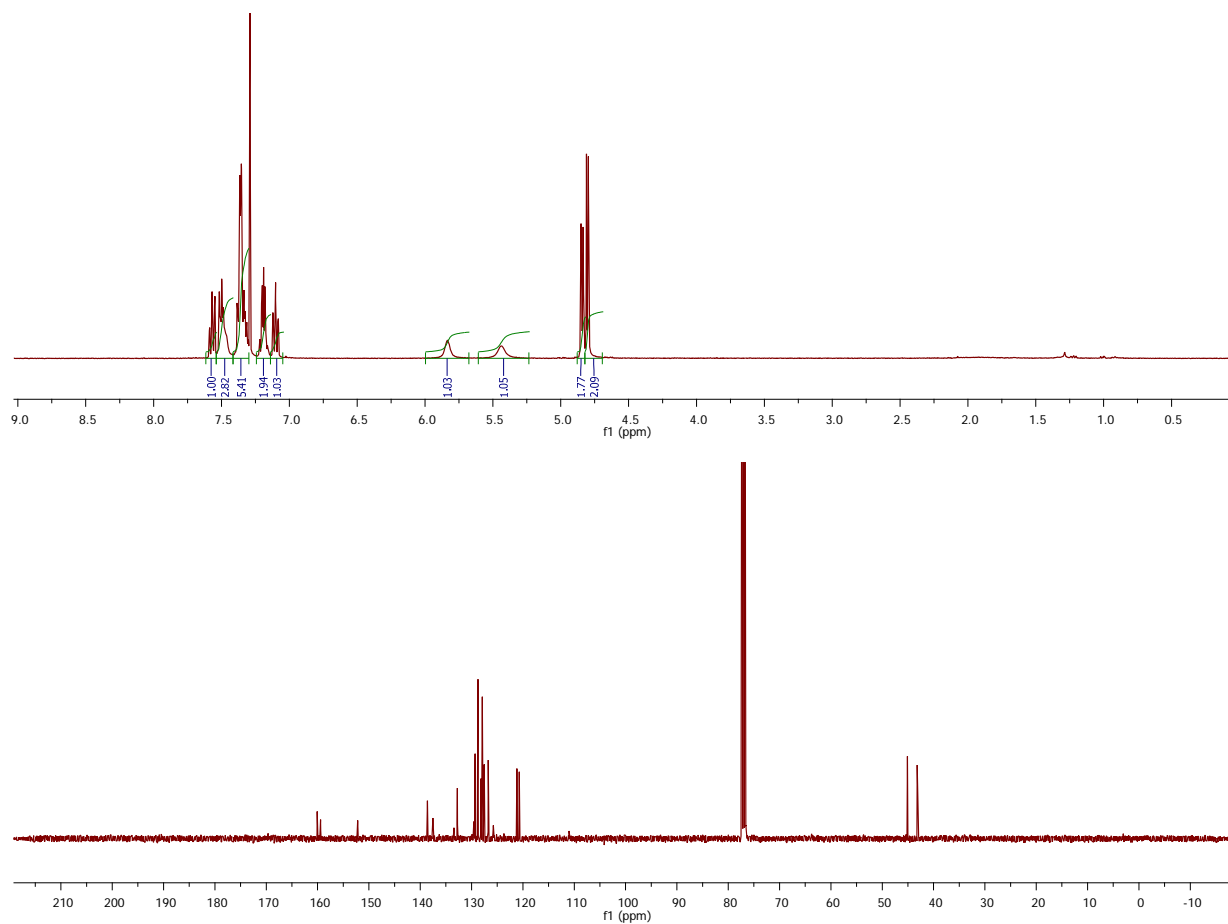
***N*⁴-Benzyl-*N*²-(2-methylbenzyl)quinazoline-2,4-diamine (S113).** Yield: 25.0 mg, 95%. ¹H NMR (400 MHz, CDCl₃) δ 7.59 – 7.52 (m, 3H), 7.43 – 7.30 (m, 6H), 7.25 – 7.13 (m, 3H), 7.13 – 7.04 (m, 1H), 5.93 (s, br. 1H), 5.19 (s, br. 1H), 4.80 (d, *J* = 5.4 Hz, 2H), 4.72 (d, *J* = 5.0 Hz, 2H), 2.40 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.2, 138.7, 137.6, 136.4, 132.8, 130.3, 128.8, 128.3, 128.0, 127.6, 127.2, 126.0, 125.7, 121.1, 120.8, 111.1, 45.1, 43.7, 19.1. HRMS (*m/z*): calcd for C₂₃H₂₃N₄ (M+H) 355.1923; found 355.1920.

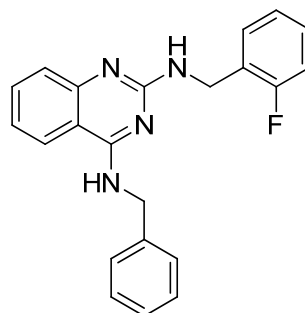




KSC-16-31

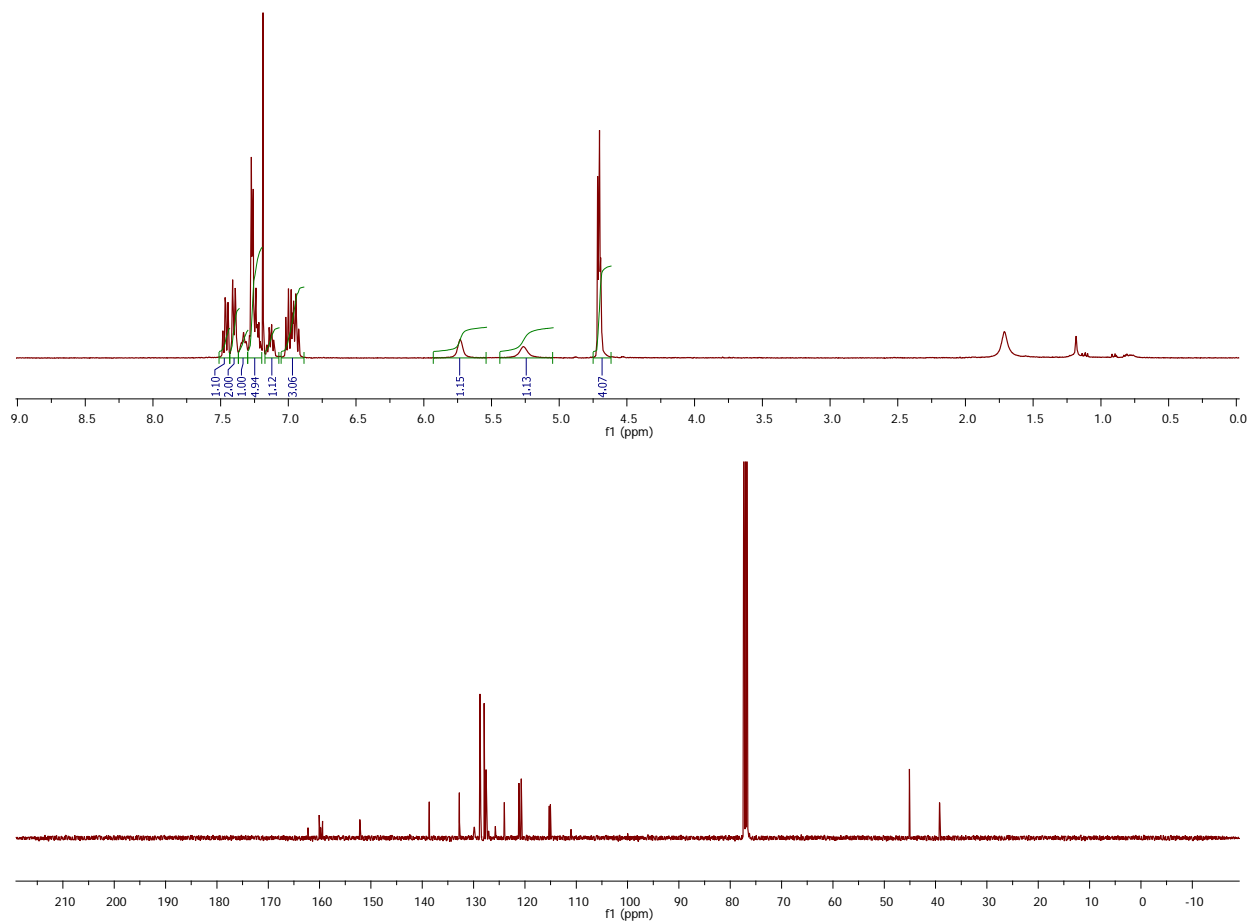
***N*⁴-Benzyl-*N*²-(2-chlorobenzyl)quinazoline-2,4-diamine (S114).** Yield: 27.0 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.54 (m, 1H), 7.50 (dd, *J* = 4.1, 7.7 Hz, 3H), 7.42 – 7.30 (m, 6H), 7.24 – 7.14 (m, 2H), 7.10 (ddd, *J* = 1.2, 6.8, 8.1 Hz, 1H), 5.83 (s, br. 1H), 5.44 (s, br. 1H), 4.84 (d, *J* = 6.3 Hz, 2H), 4.80 (d, *J* = 5.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.2, 138.6, 137.6, 133.4, 132.8, 129.6, 129.3, 128.8, 128.2, 127.9, 127.5, 126.8, 125.8, 121.2, 120.7, 111.0, 45.1, 43.2. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+H) 375.1376; found 375.1376.

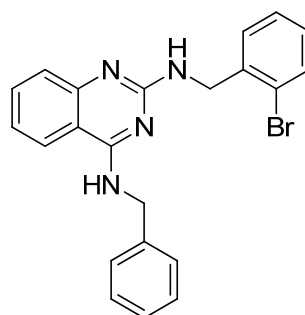




KSC-16-35

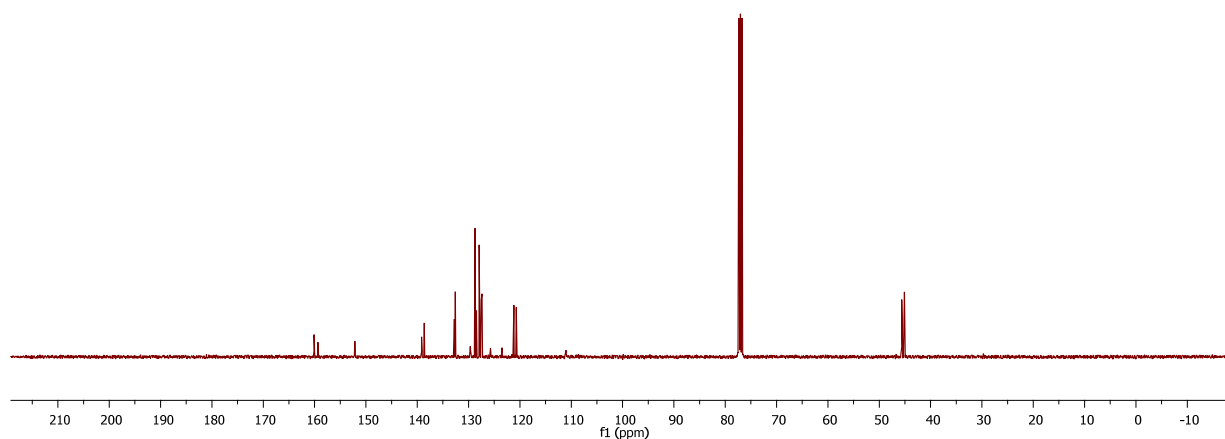
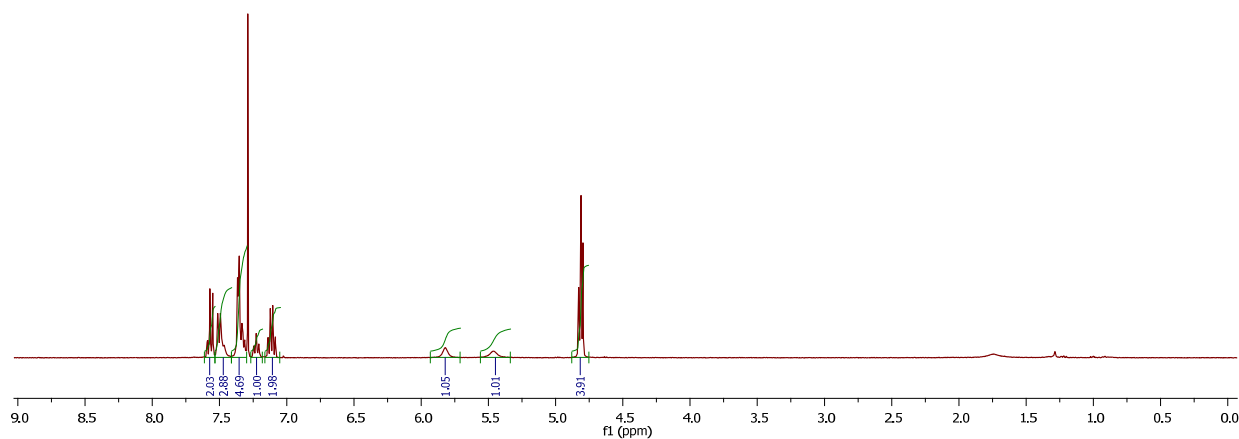
***N*⁴-Benzyl-*N*²-(2-fluorobenzyl)quinazoline-2,4-diamine (S115).** Yield: 26.5 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.51 – 7.43 (m, 1H), 7.40 (d, *J* = 7.9 Hz, 2H), 7.33 (s, 1H), 7.30 – 7.20 (m, 5H), 7.17 – 7.07 (m, 1H), 7.05 – 6.88 (m, 3H), 5.73 (s, br. 1H), 5.27 (s, br. 1H), 4.72 – 4.69 (m, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 162.3, 160.1, 159.8, 159.4, 152.2, 138.6, 132.8, 129.9, 128.8, 128.6, 128.5, 127.9, 127.6, 127.2, 127.0, 125.7, 124.0, 124.0, 121.2, 120.7, 115.3, 115.0, 111.0, 45.1, 39.24, 39.20. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (M+H) 359.1672; found 359.1672.

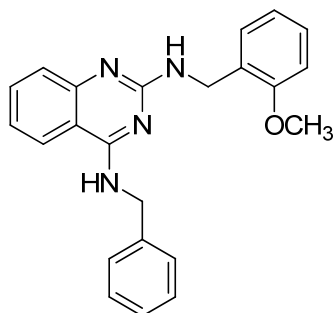




KSC-16-40

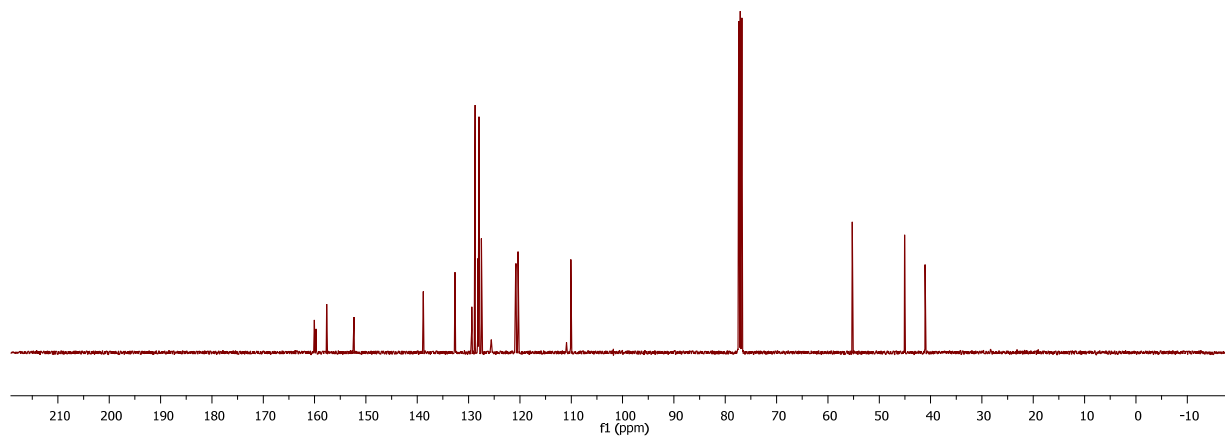
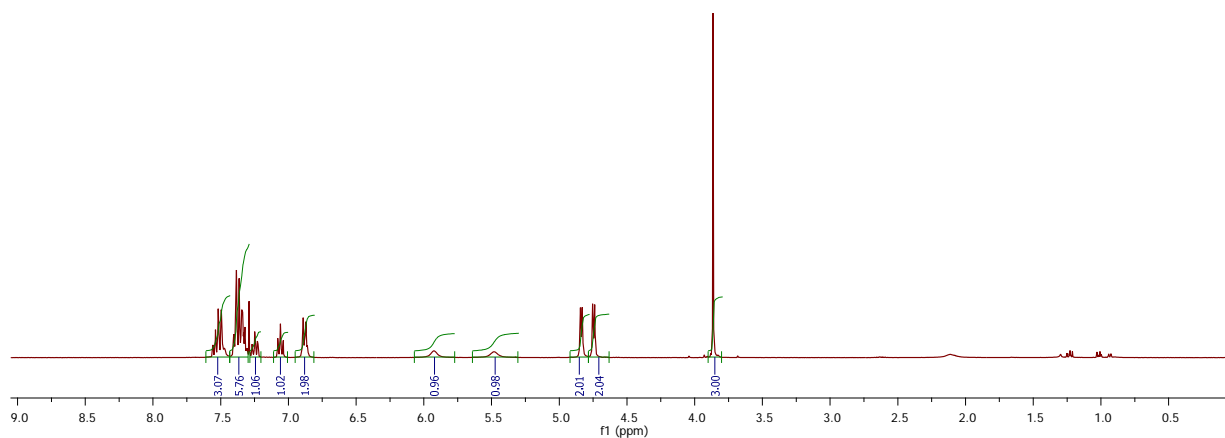
***N*⁴-Benzyl-*N*²-(2-bromobenzyl)quinazoline-2,4-diamine (S116).** Yield: 31.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.58 (dd, *J* = 4.9, 11.7 Hz, 2H), 7.51 – 7.46 (m, 3H), 7.36 – 7.31 (m, 5H), 7.23 (t, *J* = 7.3 Hz, 1H), 7.16 – 7.05 (m, 2H), 5.82 (s, br. 1H), 5.47 (s, br. 1H), 4.82 (d, *J* = 6.4 Hz, 2H), 4.81 (d, *J* = 6.4 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.2, 139.2, 138.6, 132.8, 132.6, 129.7, 128.8, 128.5, 127.9, 127.5, 127.4, 125.7, 123.5, 121.2, 120.7, 111.0, 45.6, 45.1. HRMS (*m/z*): calcd for C₂₂H₂₀BrN₄ (M+H) 419.0871 and 421.0851; found 419.0866.

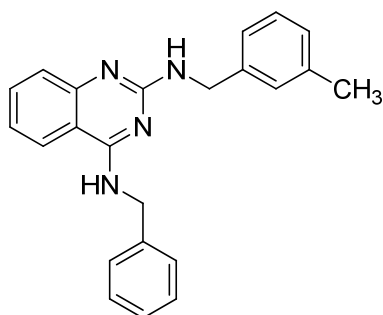




KSC-16-29

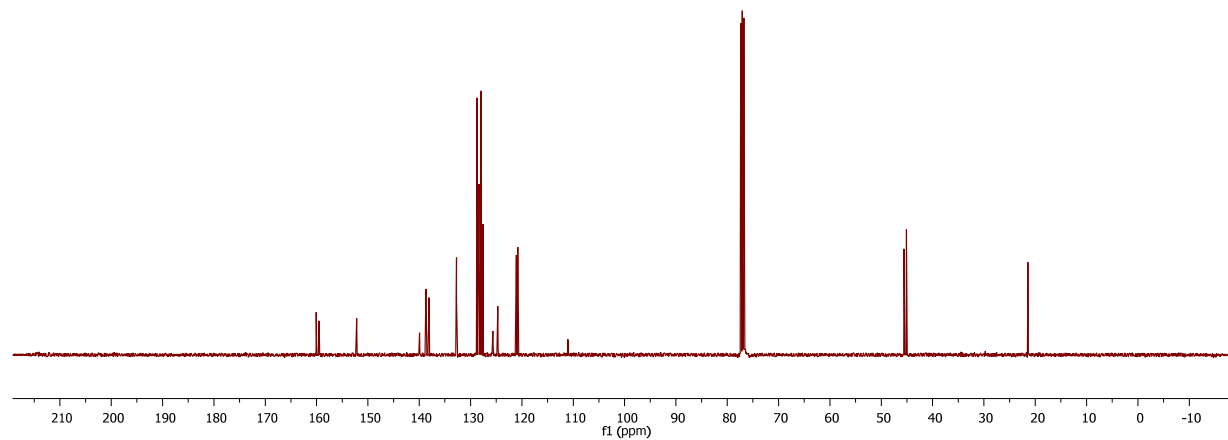
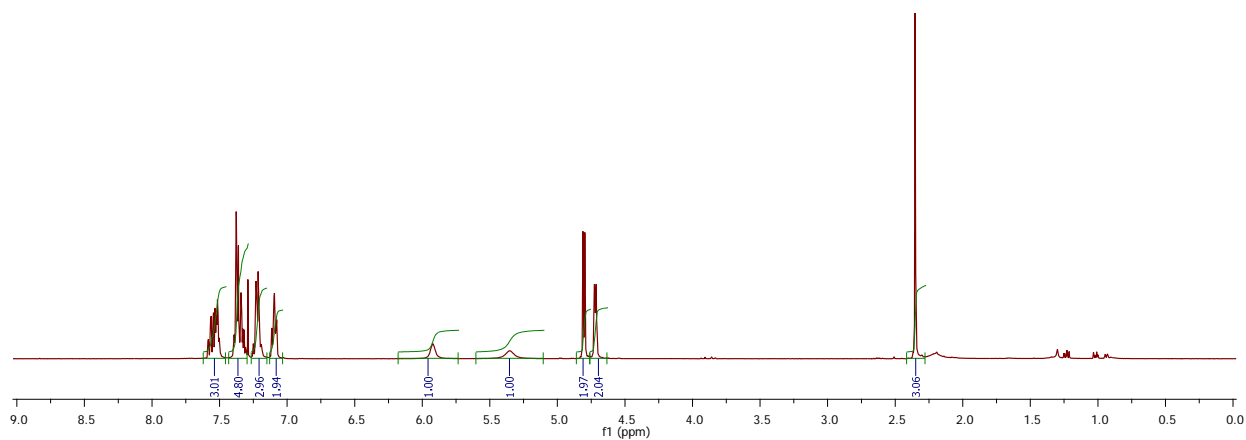
***N*⁴-Benzyl-*N*²-(2-methoxybenzyl)quinazoline-2,4-diamine (S117).** Yield: 26.4 mg, 96%. ¹H NMR (400 MHz, CDCl₃) δ 7.61 – 7.43 (m, 3H), 7.43 – 7.30 (m, 6H), 7.28 – 7.20 (m, 1H), 7.11 – 7.01 (m, 1H), 6.95 – 6.81 (m, 2H), 5.93 (s, br. 1H), 5.48 (s, br. 1H), 4.84 (d, *J* = 5.4 Hz, 2H), 4.75 (d, *J* = 6.0 Hz, 2H), 3.86 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.7, 157.6, 152.3, 138.8, 132.6, 129.4, 128.7, 128.2, 128.1, 128.0, 127.5, 125.6, 120.8, 120.8, 120.4, 110.9, 110.1, 55.3, 45.1, 41.1. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (*M*+*H*) 371.1872; found 371.1869.

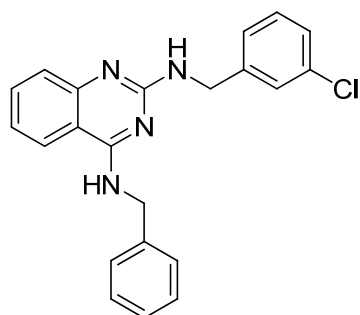




KSC-16-28

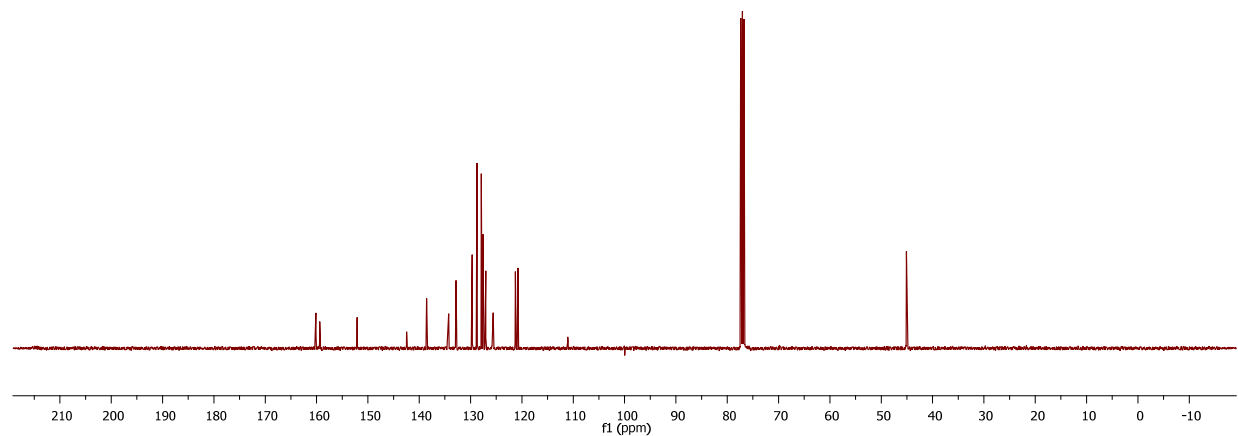
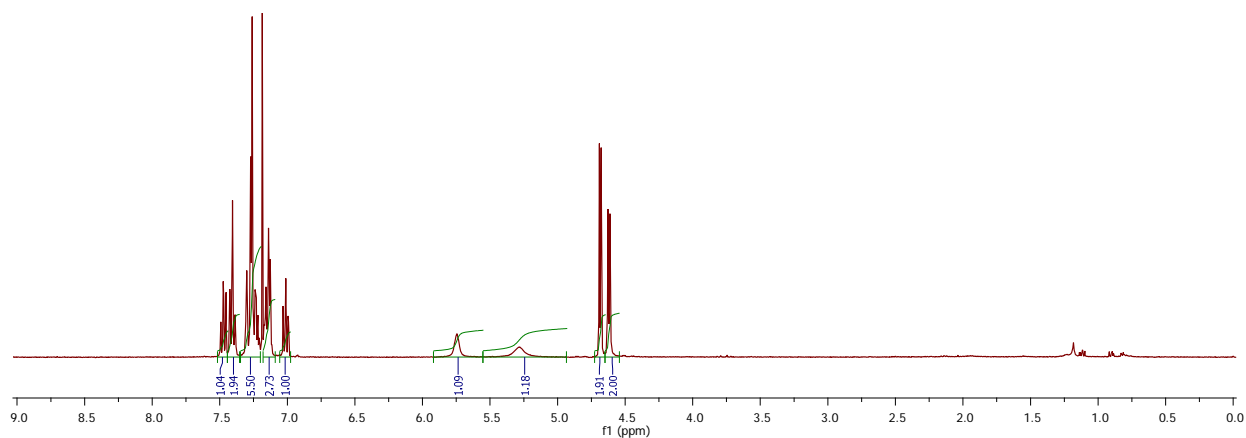
***N*⁴-Benzyl-*N*²-(3-methylbenzyl)quinazoline-2,4-diamine (S118).** Yield: 26.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.46 (m, 3H), 7.43 – 7.30 (m, 5H), 7.27 – 7.15 (m, 3H), 7.09 (ddd, *J* = 1.4, 6.7, 8.1 Hz, 2H), 5.92 (s, br. 1H), 5.35 (s, br. 1H), 4.80 (d, *J* = 5.5 Hz, 2H), 4.72 (d, *J* = 5.1 Hz, 2H), 2.35 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.5, 152.2, 140.0, 138.7, 138.1, 132.8, 128.7, 128.4, 128.0, 127.7, 127.6, 125.7, 124.7, 121.1, 120.8, 111.1, 45.6, 45.1, 21.4. HRMS (*m/z*): calcd for C₂₃H₂₃N₄ (M+H) 355.1923; found 355.1922.

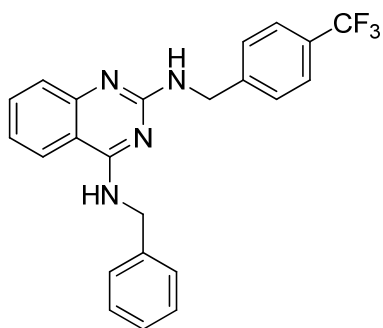




KSC-16-32

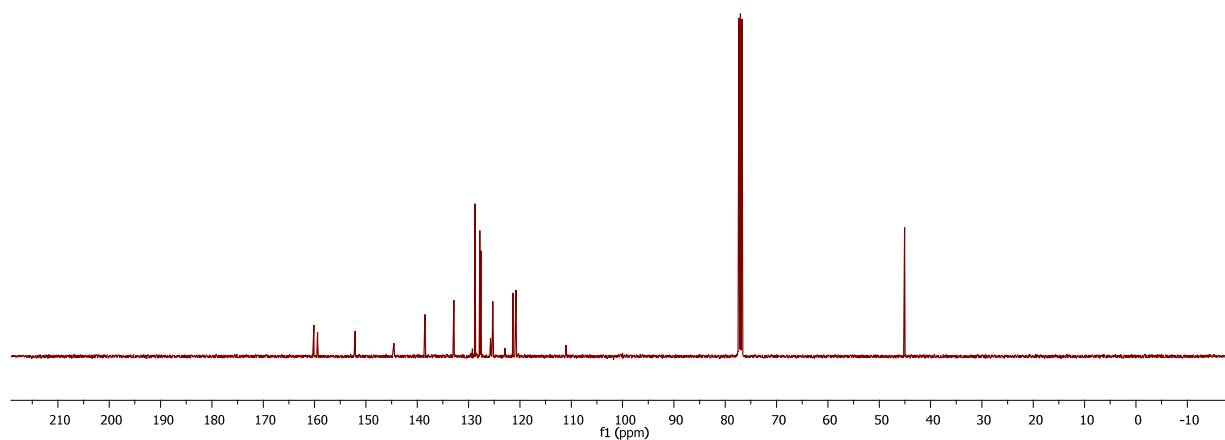
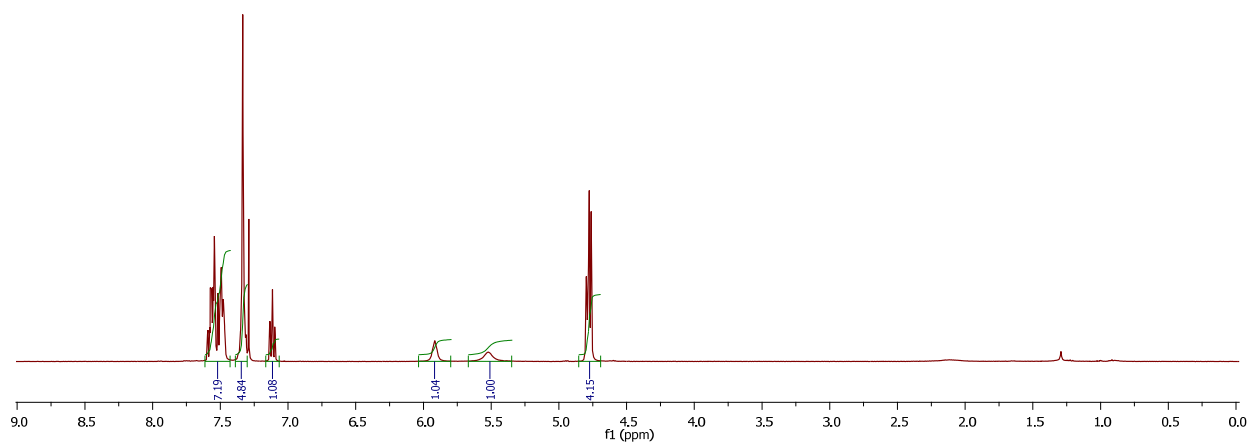
***N*⁴-Benzyl-*N*²-(3-chlorobenzyl)quinazoline-2,4-diamine (S119).** Yield: 26.4 mg, 95%. ¹H NMR (400 MHz, CDCl₃) δ 7.52 – 7.44 (m, 1H), 7.41 (t, *J* = 8.0 Hz, 2H), 7.35 – 7.20 (m, 6H), 7.18 – 7.09 (m, 3H), 7.06 – 6.98 (m, 1H), 5.75 (s, br. 1H), 5.28 (s, br. 1H), 4.68 (d, *J* = 5.5 Hz, 2H), 4.62 (d, *J* = 6.1 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.1, 142.5, 138.6, 134.3, 132.8, 129.7, 128.8, 127.9, 127.6, 127.1, 125.7, 125.6, 121.3, 120.8, 111.1, 45.1, 45.0. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+*H*) 375.1376; found 375.1375.

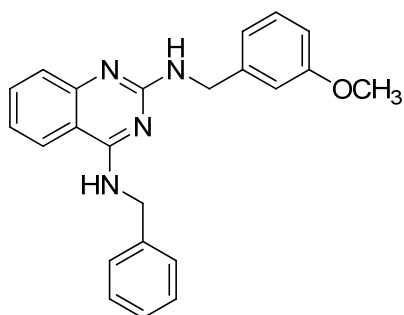




KSC-16-6

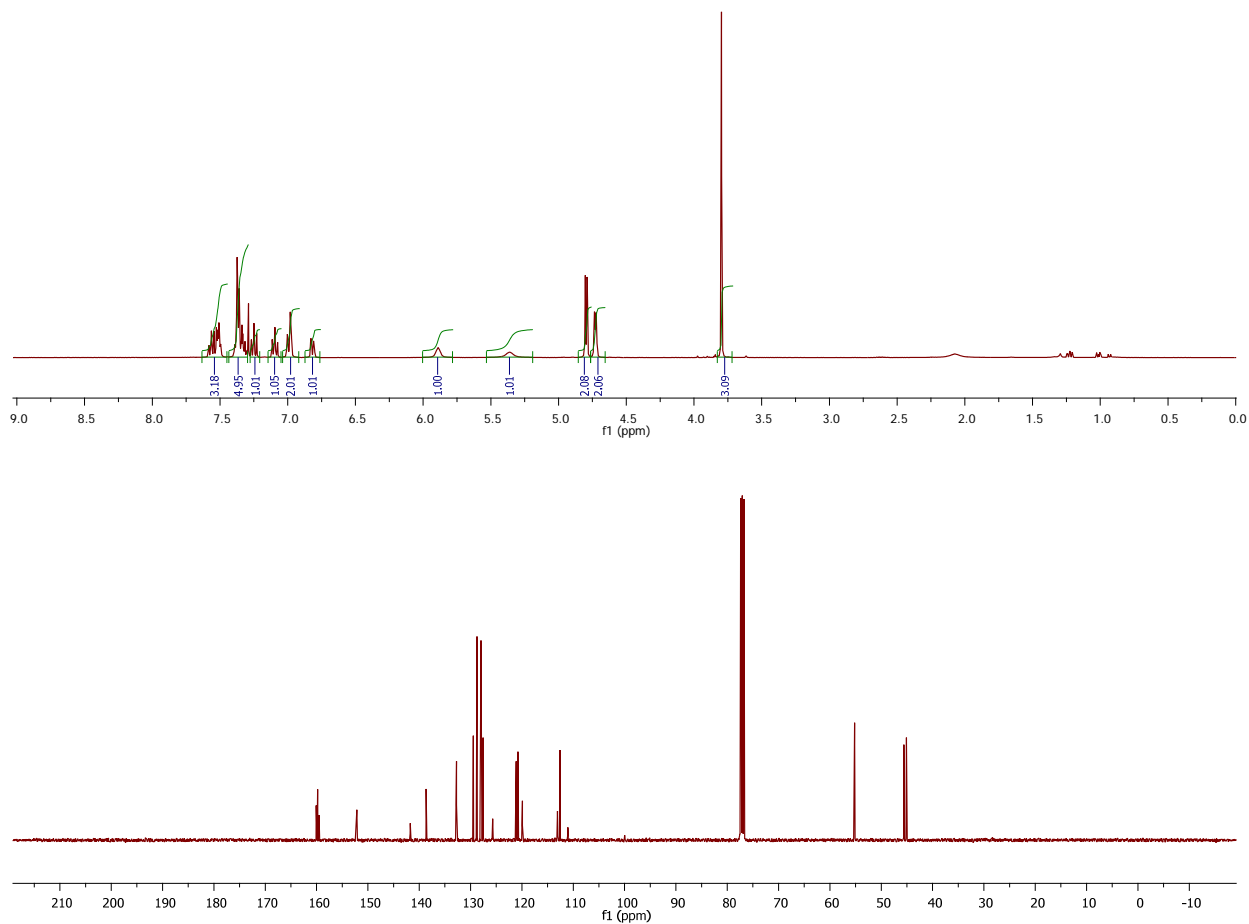
***N*⁴-Benzyl-*N*²-(4-(trifluoromethyl)benzyl)quinazoline-2,4-diamine (S120 or 46).** Yield: 30.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.59 – 7.48 (m, 7H), 7.33 – 7.31 (m, 5H), 7.11 (ddd, *J* = 1.3, 6.9, 8.2 Hz, 1H), 5.92 (s, br. 1H), 5.52 (s, br. 1H), 4.79 (d, *J* = 6.2 Hz, 2H), 4.77 (d, *J* = 5.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.1, 144.6, 138.5, 132.9, 129.2, 128.9, 128.8, 127.8, 127.6, 125.7, 125.6, 125.4, 125.34, 125.30, 125.26, 122.9, 121.4, 120.8, 111.1, 45.05. HRMS (*m/z*): calcd for C₂₃H₂₀F₃N₄ (*M*+*H*) 409.1640; found 409.1637.

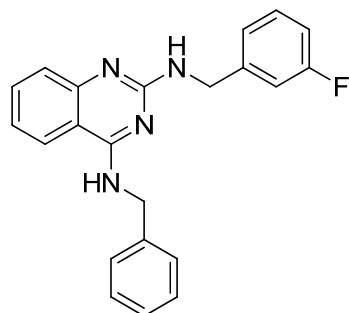




KSC-16-30

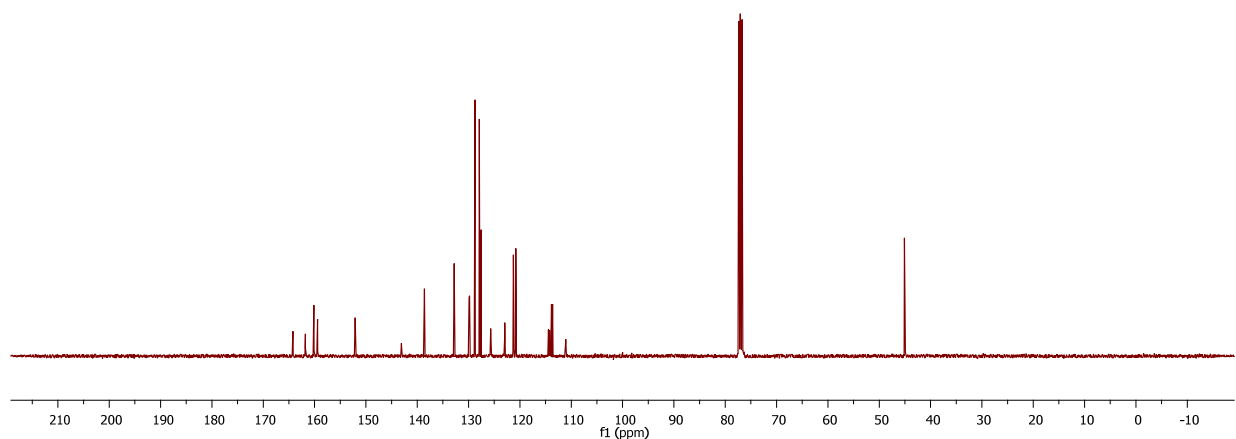
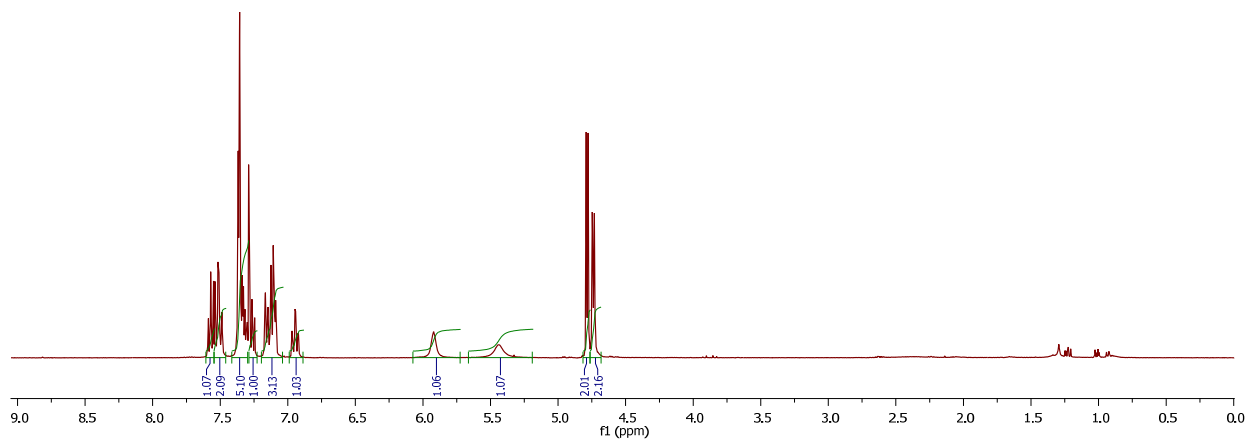
***N*⁴-Benzyl-*N*²-(3-methoxybenzyl)quinazoline-2,4-diamine (S121 or 47).** Yield: 27.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.63 – 7.45 (m, 3H), 7.43 – 7.30 (m, 5H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.09 (ddd, *J* = 1.3, 6.8, 8.1 Hz, 1H), 6.99 (d, *J* = 8.1 Hz, 2H), 6.82 (dd, *J* = 1.9, 8.2 Hz, 1H), 5.89 (s, br. 1H), 5.36 (s, br. 1H), 4.80 (d, *J* = 5.5 Hz, 2H), 4.73 (d, *J* = 5.1 Hz, 2H), 3.80 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.8, 159.5, 152.2, 141.8, 138.7, 132.8, 129.5, 128.7, 128.0, 127.6, 125.7, 121.1, 120.8, 119.9, 113.1, 112.6, 111.1, 55.2, 45.6, 45.1. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (M+H) 371.1872; found 371.1870.

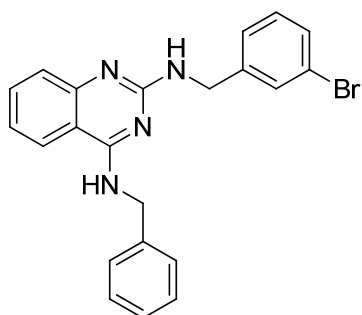




KSC-16-36

***N*⁴-Benzyl-*N*²-(3-fluorobenzyl)quinazoline-2,4-diamine (S122 or 48).** Yield: 25.0 mg, 94%. ¹H NMR (400 MHz, CDCl₃) δ 7.57 (ddd, *J* = 1.3, 6.8, 8.2 Hz, 1H), 7.51 (dd, *J* = 8.3, 11.7 Hz, 2H), 7.42 – 7.30 (m, 5H), 7.29 – 7.23 (m, 1H), 7.20 – 7.04 (m, 3H), 6.94 (td, *J* = 1.9, 8.3 Hz, 1H), 5.92 (s, br. 1H), 5.44 (s, br. 1H), 4.78 (d, *J* = 5.5 Hz, 2H), 4.74 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 164.2, 161.8, 160.1, 159.4, 152.1, 143.1, 143.0, 138.6, 132.8, 129.9, 129.8, 128.8, 127.9, 127.6, 125.7, 123.0, 121.3, 120.8, 114.4, 114.2, 113.8, 113.6, 111.1, 45.1, 45.02, 45.00. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1671.

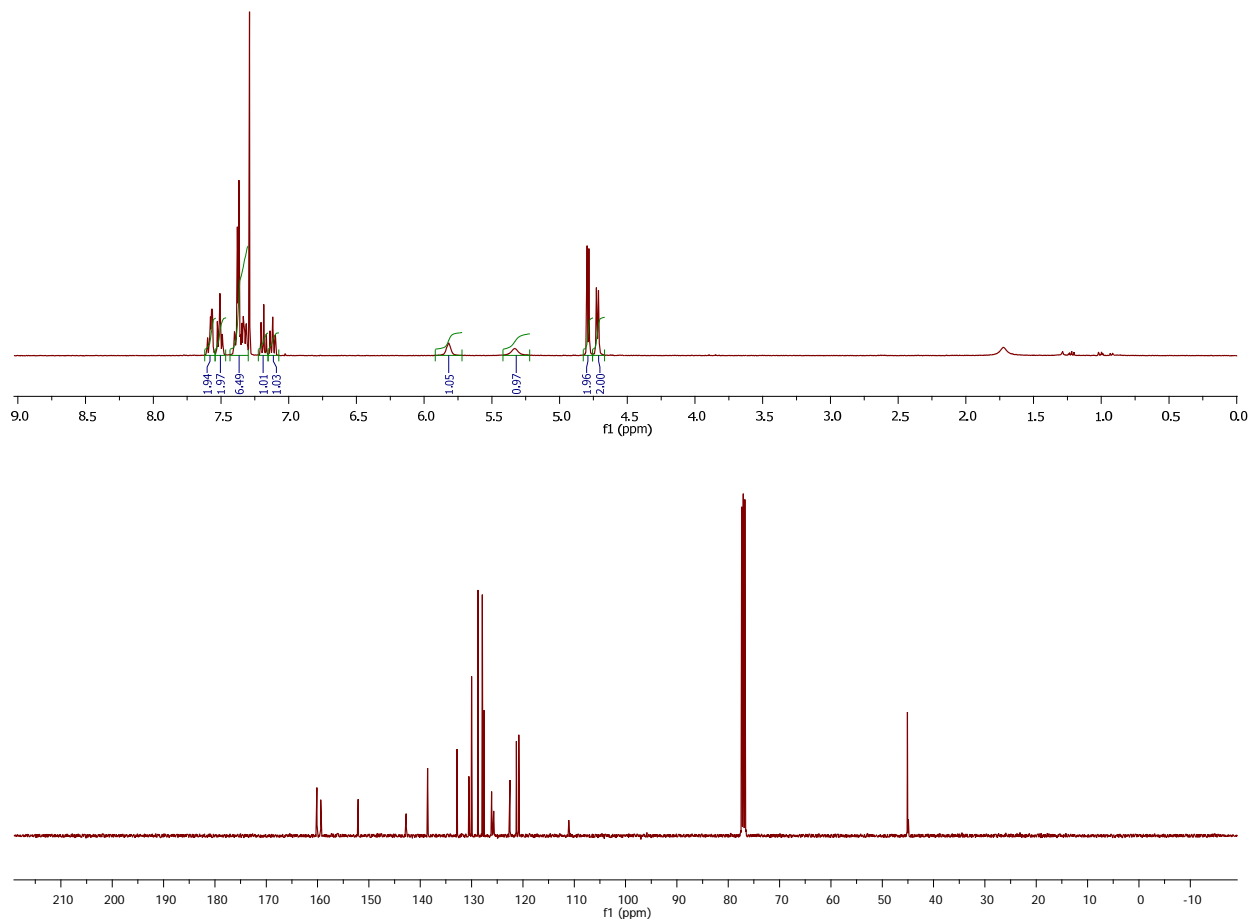


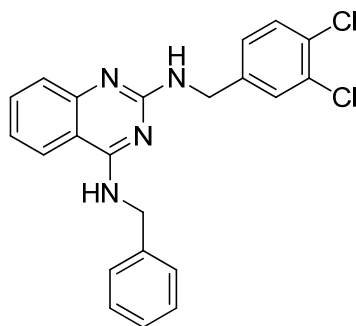


KSC-16-41

***N*⁴-Benzyl-*N*²-(3-bromobenzyl)quinazoline-2,4-diamine (S123 or 49).** Yield: 29.4 mg, 95%.

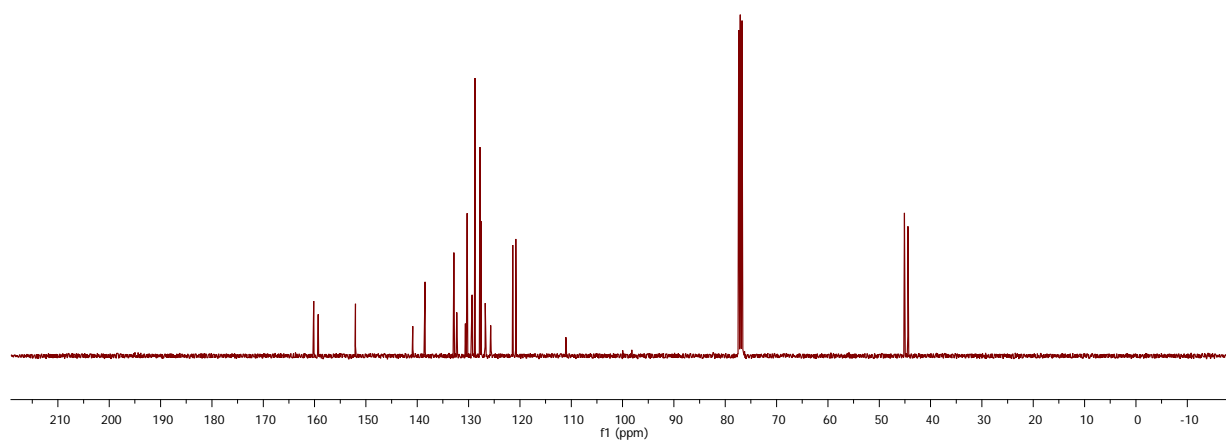
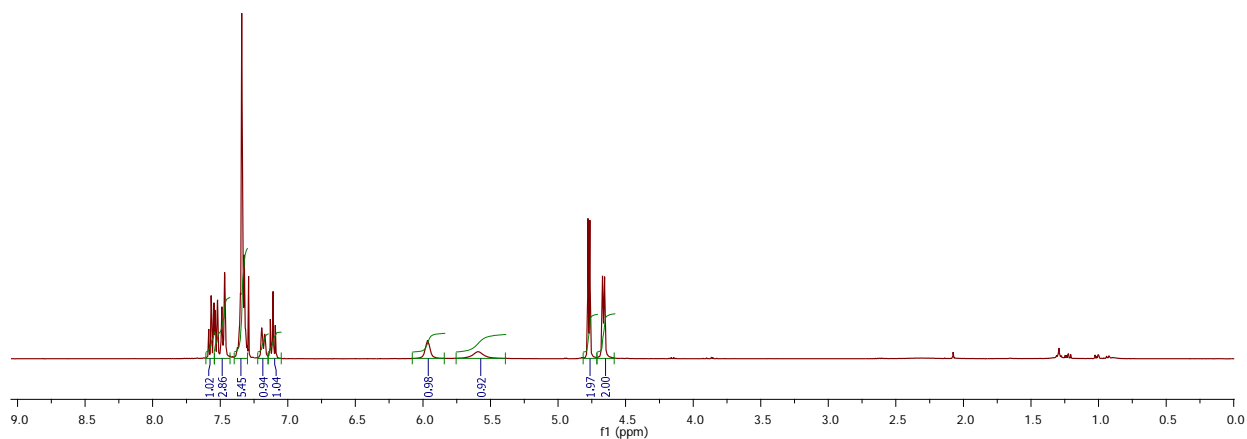
¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.54 (m, 2H), 7.51 (t, *J* = 7.4 Hz, 2H), 7.43 – 7.30 (m, 7H), 7.18 (t, *J* = 7.8 Hz, 1H), 7.15 – 7.07 (m, 1H), 5.82 (s, br. 1H), 5.33 (s, br. 1H), 4.79 (d, *J* = 5.4 Hz, 2H), 4.72 (d, *J* = 6.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.4, 152.1, 142.8, 138.6, 132.8, 130.5, 130.0, 128.8, 127.9, 127.6, 126.1, 125.7, 122.5, 121.3, 120.8, 111.1, 45.1, 44.9. HRMS (*m/z*): calcd for C₂₂H₂₀BrN₄ (M+H) 419.0871 and 421.0851; found 419.0866.

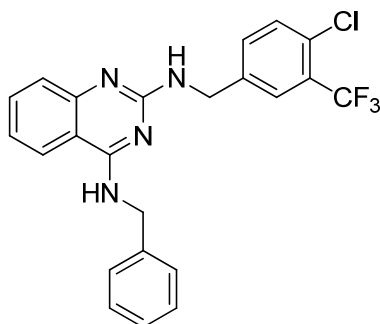




KSC-16-3

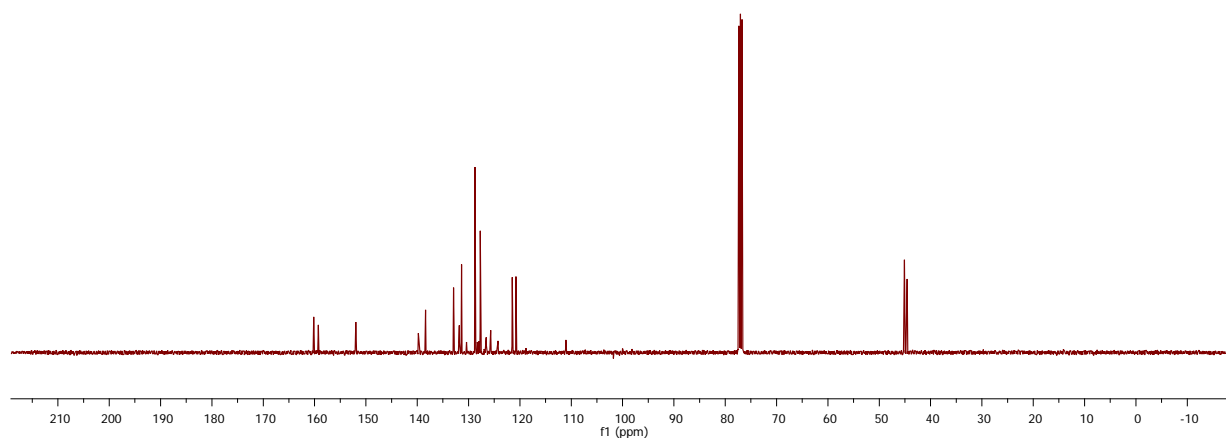
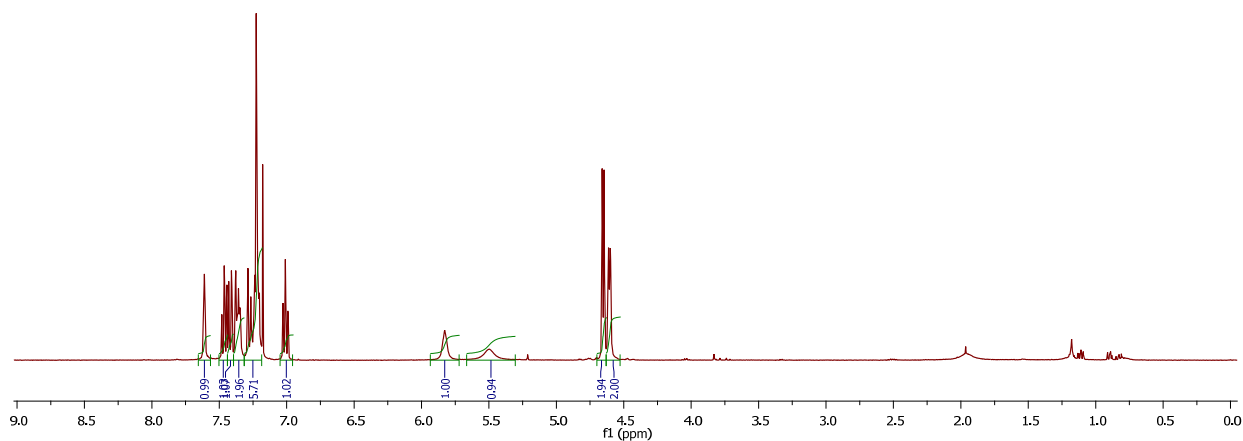
***N*⁴-Benzyl-*N*²-(3,4-dichlorobenzyl)quinazoline-2,4-diamine (S124).** Yield: 30.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.57 (ddd, *J* = 1.4, 6.9, 8.3 Hz, 1H), 7.54 – 7.47 (m, 3H), 7.40 – 7.30 (m, 6H), 7.18 (d, *J* = 8.1 Hz, 1H), 7.11 (ddd, *J* = 1.3, 6.9, 8.2 Hz, 1H), 5.97 (s, br. 1H), 5.59 (s, br. 1H), 4.77 (d, *J* = 5.5 Hz, 2H), 4.66 (d, *J* = 6.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 159.3, 152.0, 140.9, 138.5, 132.9, 132.3, 130.6, 130.3, 129.3, 128.8, 127.8, 127.6, 126.8, 125.7, 121.4, 120.8, 111.1, 45.1, 44.4. HRMS (*m/z*): calcd for C₂₂H₁₉Cl₂N₄ (*M*+H) 409.0987; found 409.0980.

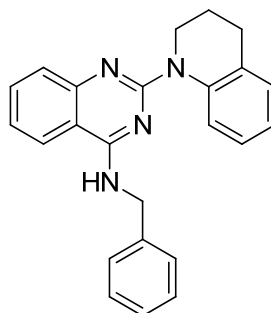




KSC-16-4

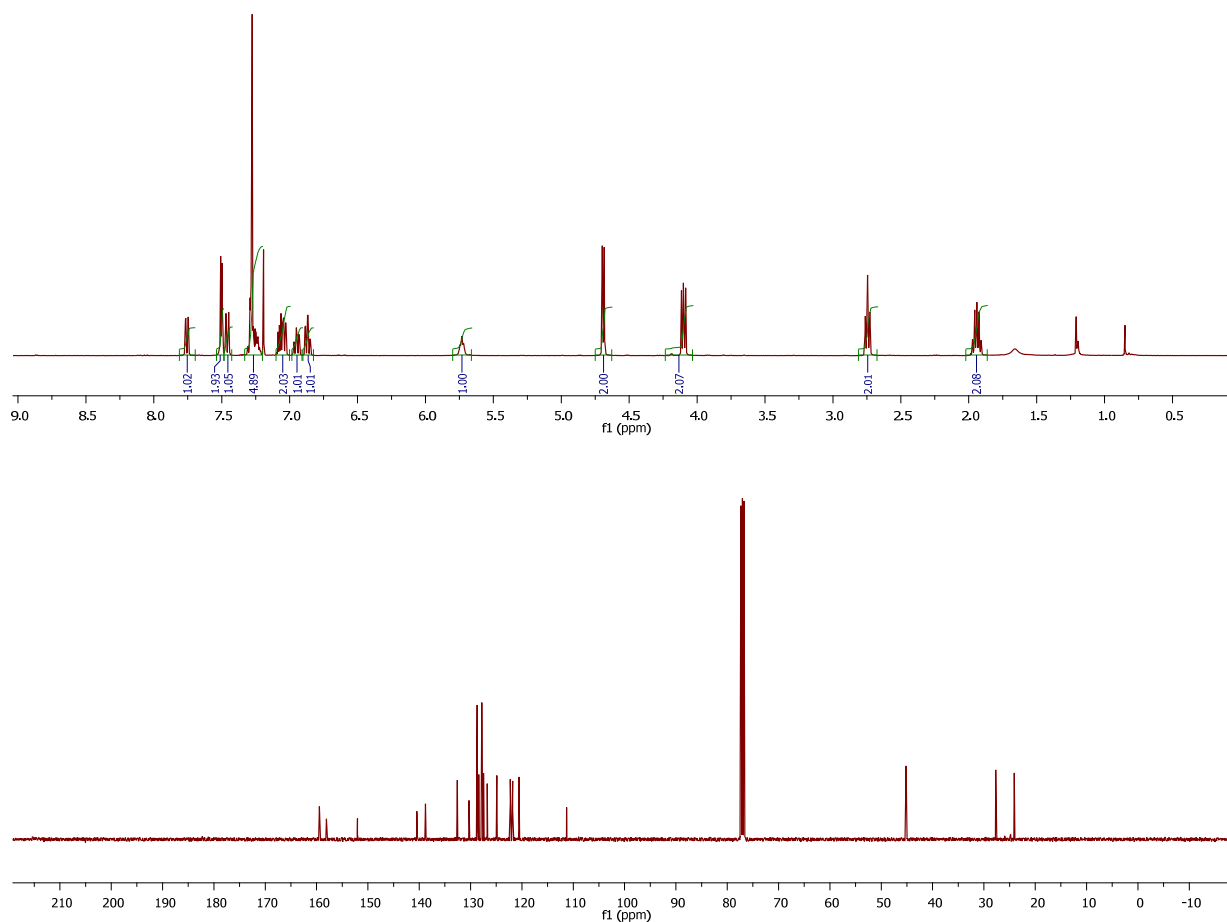
***N*⁴-Benzyl-*N*²-(4-chloro-3-(trifluoromethyl)benzyl)quinazoline-2,4-diamine (S125).** Yield: 32.0 mg, 97%. ¹H NMR (400 MHz, CDCl₃) δ 7.61 (s, 1H), 7.46 (ddd, *J* = 1.4, 6.9, 8.3 Hz, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.32 – 7.19 (m, 6H), 7.01 (ddd, *J* = 1.2, 6.9, 8.2 Hz, 1H), 5.83 (s, br. 1H), 5.50 (s, br. 1H), 4.65 (d, *J* = 5.5 Hz, 2H), 4.61 (d, *J* = 5.5 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 159.3, 152.0, 139.8, 138.4, 132.9, 131.8, 131.4, 130.4, 128.8, 128.3, 128.0, 127.7, 127.6, 126.62, 126.58, 125.7, 124.3, 121.6, 121.5, 120.8, 111.1, 45.1, 44.6. HRMS (*m/z*): calcd for C₂₃H₁₉ClF₃N₄ (*M*+*H*) 443.1250; found 443.1246.

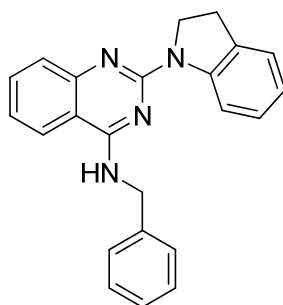




KSC-16-125

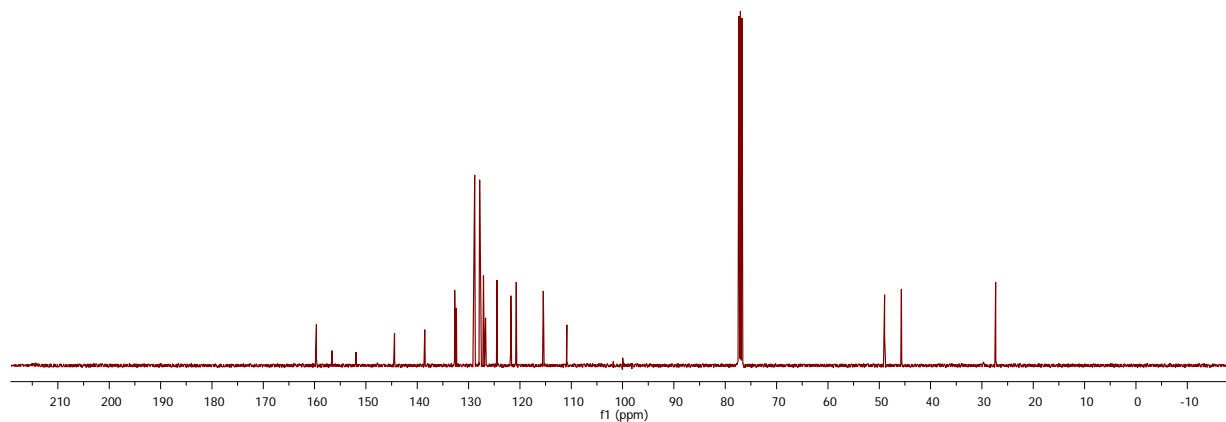
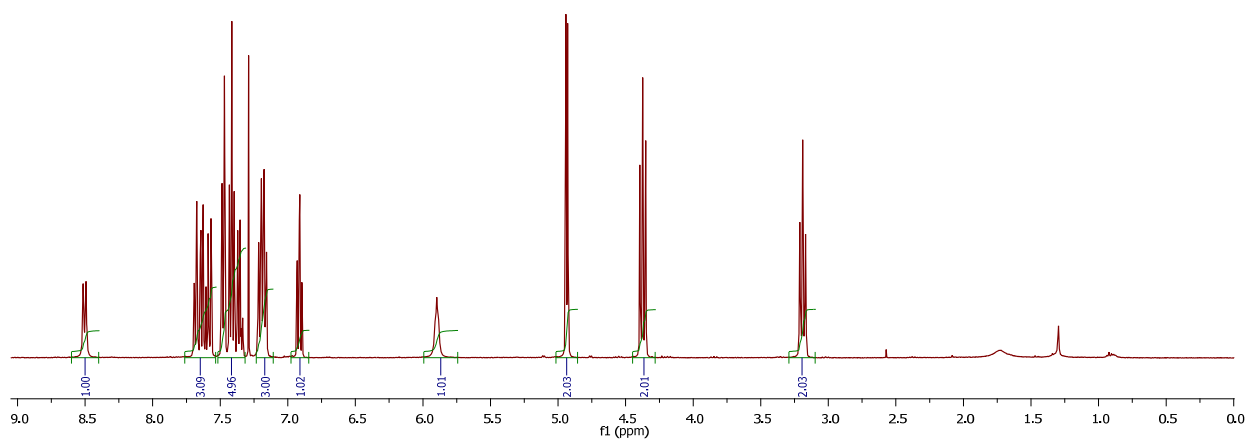
***N*-Benzyl-2-(3,4-dihydroquinolin-1(2*H*)-yl)quinazolin-4-amine (S142).** Yield: 12.4 mg, 91%. ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 7.2$ Hz, 1H), 7.50 (dd, $J = 1.0, 4.5$ Hz, 2H), 7.46 (d, $J = 8.2$ Hz, 1H), 7.33 – 7.20 (m, 5H), 7.10 – 7.00 (m, 2H), 6.94 (dd, $J = 4.1, 11.4$ Hz, 1H), 6.87 (td, $J = 1.2, 7.3$ Hz, 1H), 5.73 (s, br. 1H), 4.69 (d, $J = 5.5$ Hz, 2H), 4.23 – 4.03 (m, 2H), 2.75 (t, $J = 6.6$ Hz, 2H), 1.94 (dt, $J = 6.6, 12.7$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.5, 158.1, 152.0, 140.5, 138.8, 132.6, 130.3, 128.7, 128.4, 127.8, 127.5, 126.8, 125.1, 124.9, 122.3, 121.8, 120.6, 111.3, 45.2, 45.1, 27.7, 24.1. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4$ ($\text{M}+\text{H}$) 367.1923; found 367.1917.

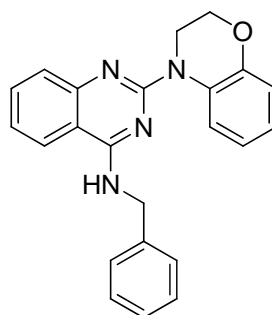




KSC-16-144

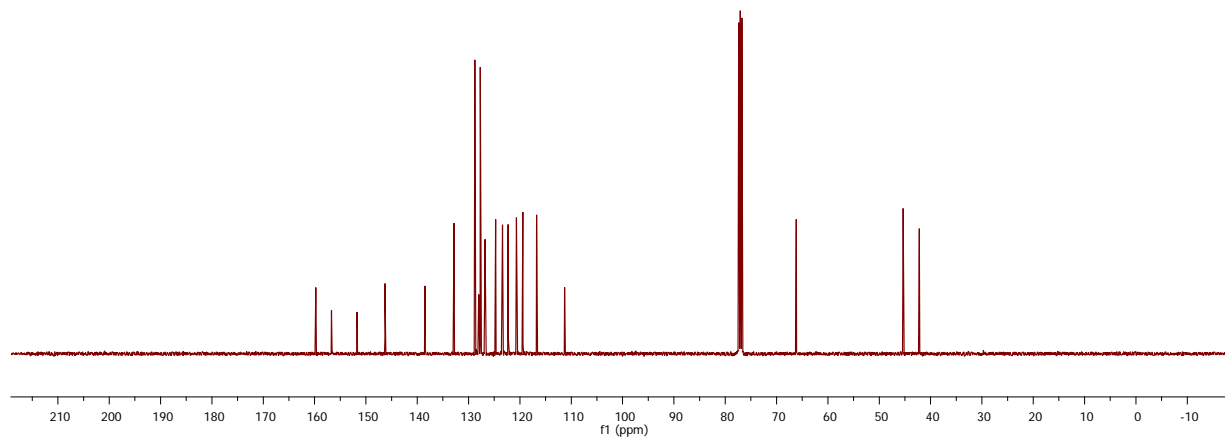
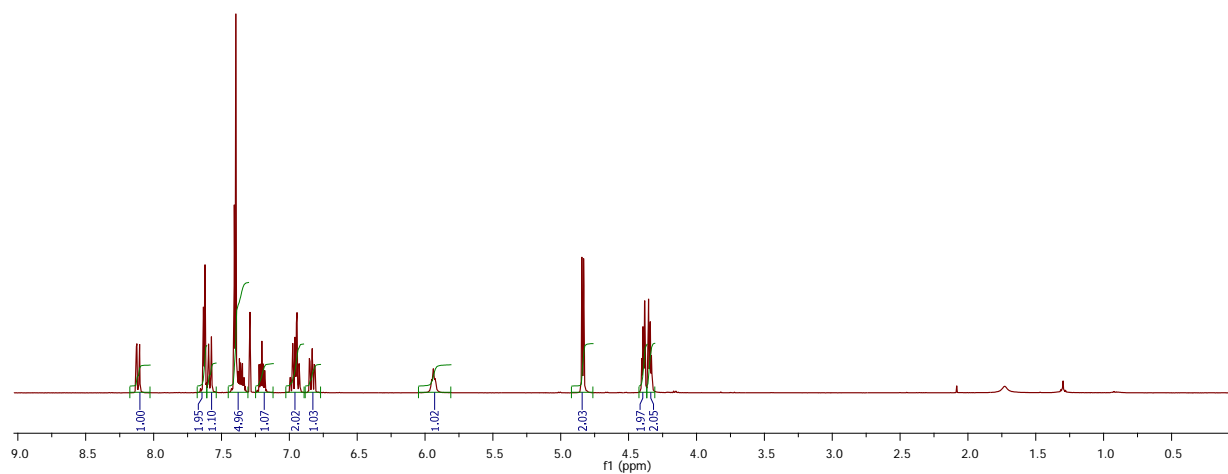
***N*-Benzyl-2-(indolin-1-yl)quinazolin-4-amine (S143).** Yield: 13.0 mg, 99%. ^1H NMR (400 MHz, CDCl_3) δ 8.50 (d, $J = 8.0$ Hz, 1H), 7.76 – 7.53 (m, 3H), 7.52 – 7.32 (m, 5H), 7.23 – 7.11 (m, 3H), 6.91 (t, $J = 7.4$ Hz, 1H), 5.90 (s, 1H), 4.94 (d, $J = 5.4$ Hz, 2H), 4.45 – 4.28 (m, 2H), 3.19 (t, $J = 8.7$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.7, 156.6, 151.9, 144.4, 138.6, 132.7, 132.4, 128.8, 127.9, 127.6, 127.1, 126.7, 124.5, 121.8, 120.8, 120.7, 115.4, 110.9, 49.0, 45.7, 27.3. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{21}\text{N}_4$ ($\text{M}+\text{H}$) 353.1766; found 353.1761.

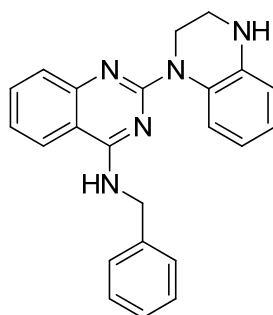




KSC-16-70

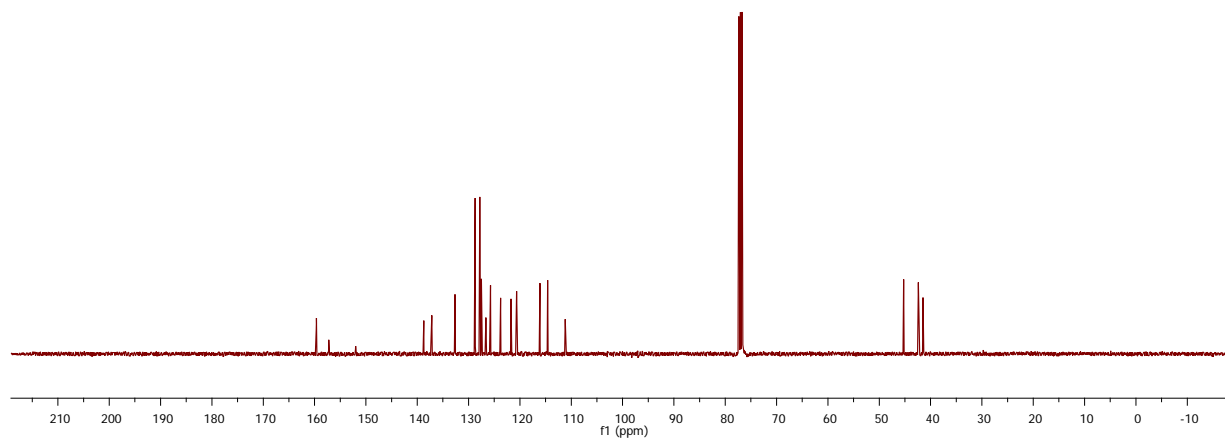
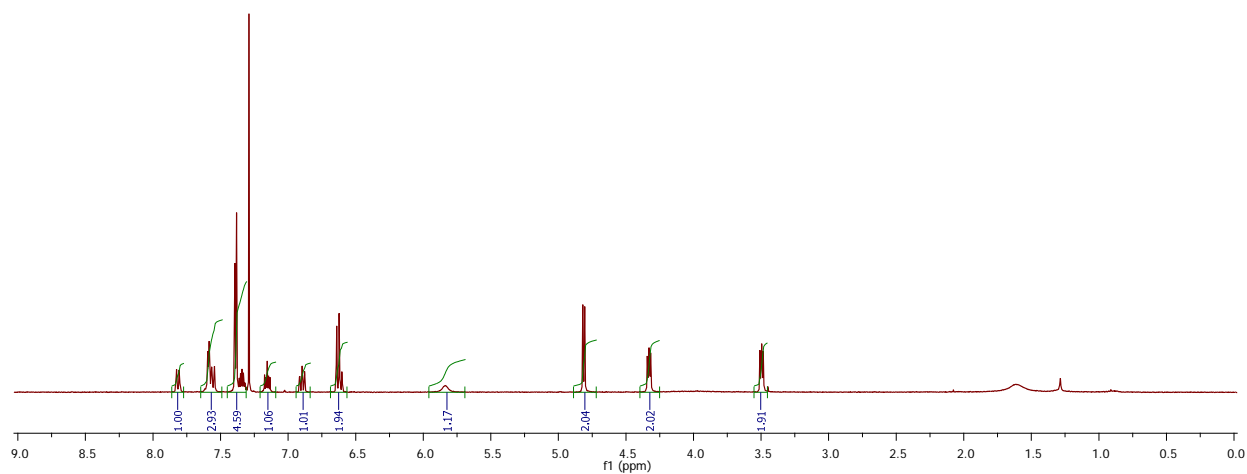
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-benzylquinazolin-4-amine (S144 or 15). Yield: 27.0 mg, 99%. ^1H NMR (400 MHz, CDCl_3) δ 8.12 (d, J = 8.3 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.58 (d, J = 8.2 Hz, 1H), 7.45 – 7.30 (m, 5H), 7.25 – 7.12 (m, 1H), 7.03 – 6.89 (m, 2H), 6.88 – 6.77 (m, 1H), 5.94 (s, 1H), 4.84 (d, J = 5.5 Hz, 2H), 4.39 (dd, J = 3.1, 5.1 Hz, 2H), 4.34 (dd, J = 3.1, 5.0 Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.8, 156.7, 151.7, 146.3, 138.5, 132.8, 128.8, 128.1, 127.7, 127.6, 126.8, 124.7, 123.4, 122.3, 120.7, 119.4, 116.7, 111.3, 66.2, 45.3, 42.2. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{21}\text{N}_4\text{O}$ (M+H) 369.1715; found 369.1716.

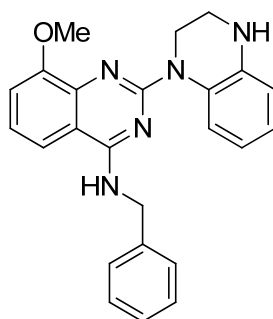




KSC-16-147

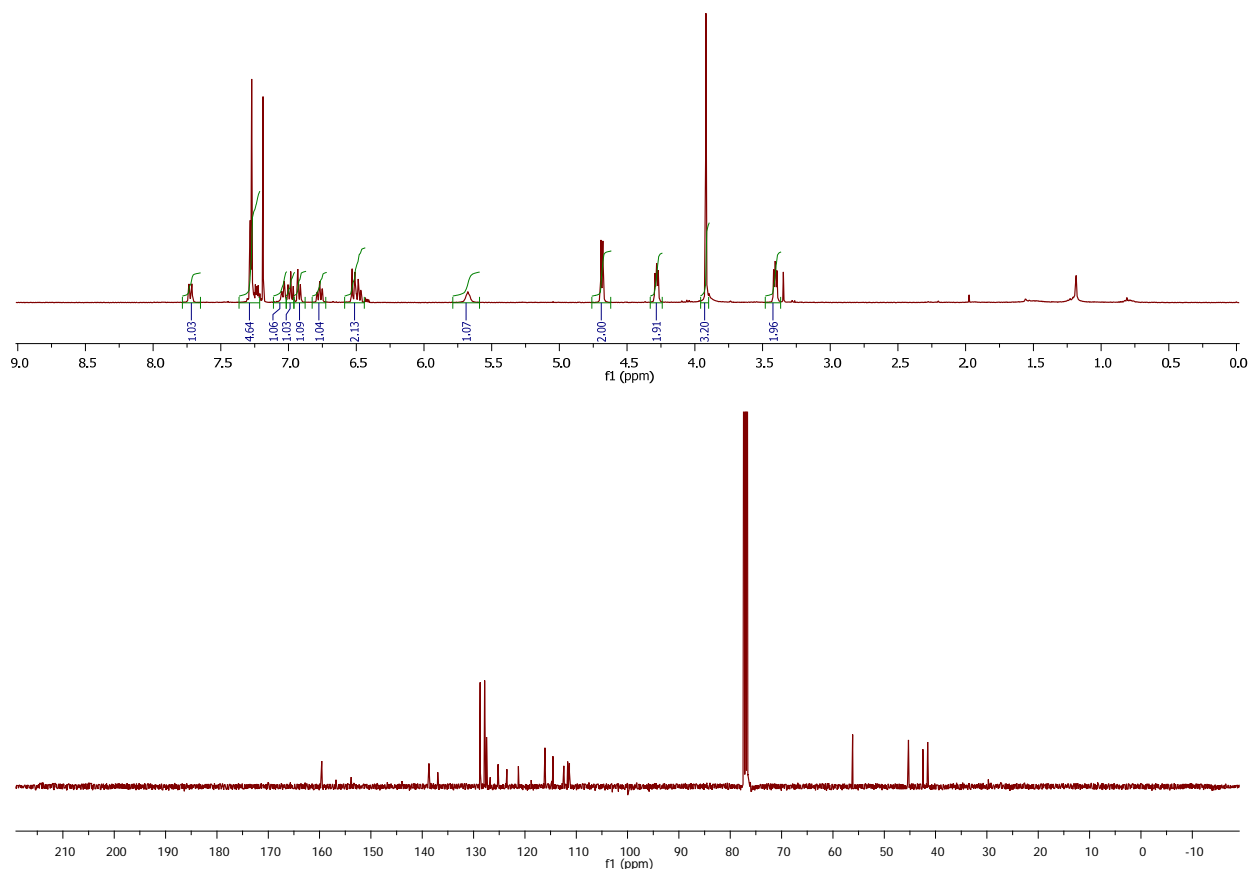
***N*-Benzyl-2-(3,4-dihydroquinoxalin-1(2*H*)-yl)quinazolin-4-amine (S145).** Yield: 13.5 mg, 99%. ^1H NMR (400 MHz, CDCl_3) δ 7.82 (d, $J = 7.8$ Hz, 1H), 7.57 (dd, $J = 6.2, 13.7$ Hz, 3H), 7.45 – 7.31 (m, 5H), 7.21 – 7.09 (m, 1H), 6.94 – 6.84 (m, 1H), 6.62 (dd, $J = 4.4, 12.2$ Hz, 2H), 5.82 (s, br. 1H), 4.81 (d, $J = 5.5$ Hz, 2H), 4.40 – 4.25 (m, 2H), 3.55 – 3.45 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.6, 157.2, 152.0, 138.7, 137.2, 132.6, 128.7, 127.8, 127.5, 126.7, 126.6, 125.7, 123.8, 121.7, 120.6, 116.1, 114.6, 111.2, 45.2, 42.4, 41.5. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{22}\text{N}_5$ ($M+H$) 368.1875; found 368.1874.

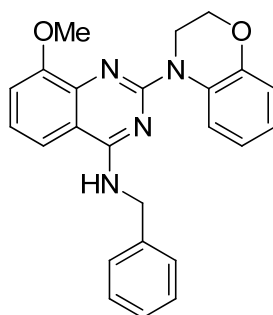




KSC-16-182

***N*-Benzyl-2-(3,4-dihydroquinoxalin-1(2*H*)-yl)-8-methoxyquinazolin-4-amine (S146).** Yield: 5.6 mg, 42%. ^1H NMR (400 MHz, CDCl_3) δ 7.72 (d, $J = 7.8$ Hz, 1H), 7.37 – 7.21 (m, 5H), 7.04 (d, $J = 7.8$ Hz, 1H), 6.98 (t, $J = 7.8$ Hz, 1H), 6.92 (d, $J = 7.7$ Hz, 1H), 6.77 (t, $J = 6.9$ Hz, 1H), 6.59 – 6.44 (m, 2H), 5.68 (s, 1H), 4.69 (d, $J = 5.4$ Hz, 2H), 4.33 – 4.24 (m, 2H), 3.92 (s, 3H), 3.48 – 3.37 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.6, 156.8, 153.8, 138.7, 137.0, 128.7, 127.9, 127.5, 126.7, 125.2, 123.5, 121.3, 118.8, 116.1, 114.5, 112.4, 111.7, 111.3, 56.2, 45.3, 42.5, 41.5. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{24}\text{N}_5\text{O}$ ($\text{M}+\text{H}$) 398.1981; found 398.1974.

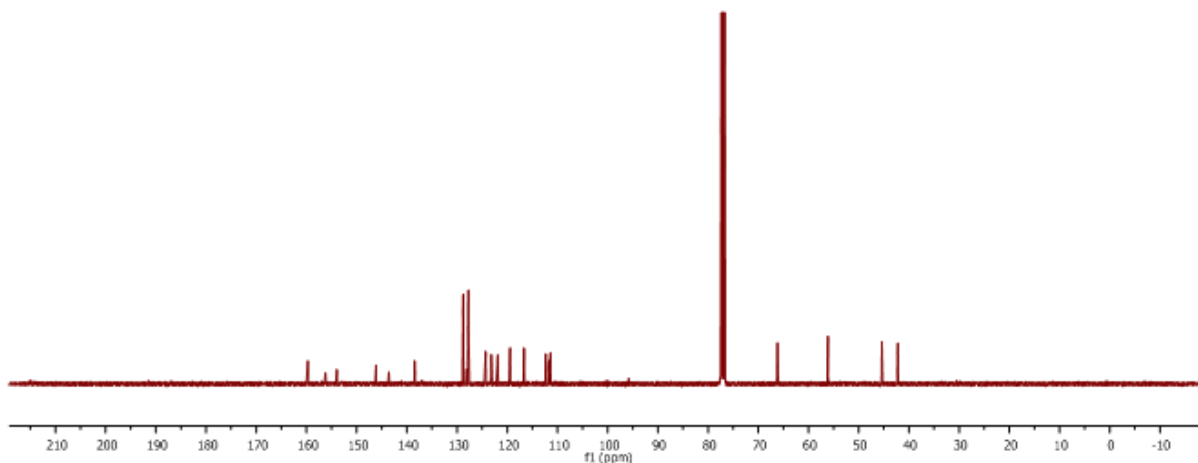
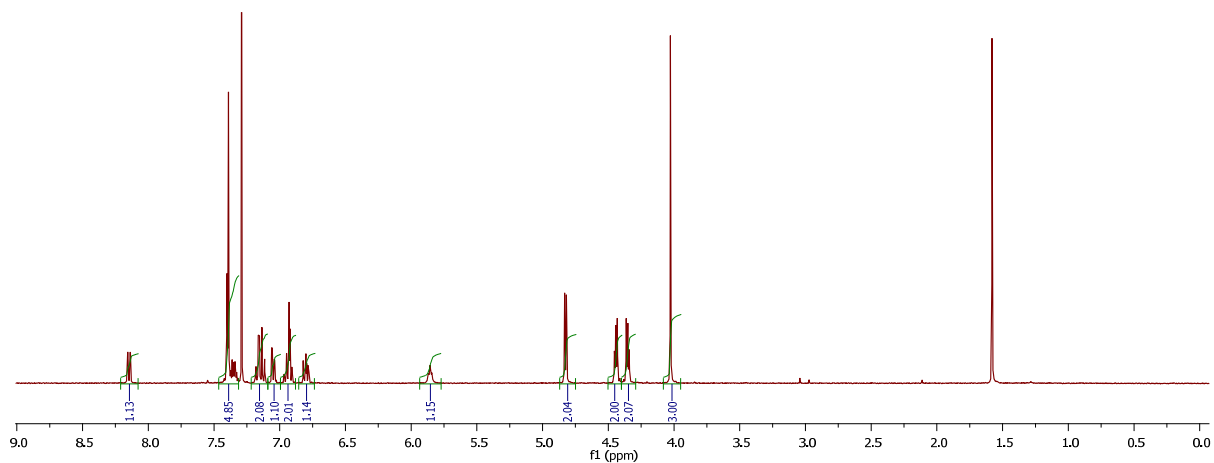


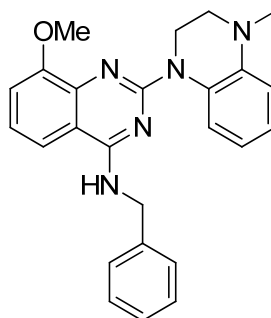


KSC-16-191

2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-benzyl-8-methoxyquinazolin-4-amine (S147 or 38).

Yield: 7.1 mg, 53%. ^1H NMR (400 MHz, CDCl_3) δ 8.21 – 8.08 (m, 1H), 7.46 – 7.31 (m, 5H), 7.18 – 7.11 (m, 2H), 7.05 (dd, $J = 1.6, 7.3$ Hz, 1H), 6.99 – 6.88 (m, 2H), 6.80 (ddd, $J = 2.3, 6.5, 8.7$ Hz, 1H), 5.86 (s, 1H), 4.83 (d, $J = 5.5$ Hz, 2H), 4.50 – 4.40 (m, 2H), 4.40 – 4.29 (m, 2H), 4.03 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.7, 156.2, 153.9, 146.2, 143.6, 138.5, 128.8, 128.1, 127.8, 127.6, 124.3, 123.2, 121.9, 119.4, 116.7, 112.3, 111.8, 111.4, 66.2, 56.1, 45.4, 42.2. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_2$ ($M+H$) 399.1821; found 399.1824.

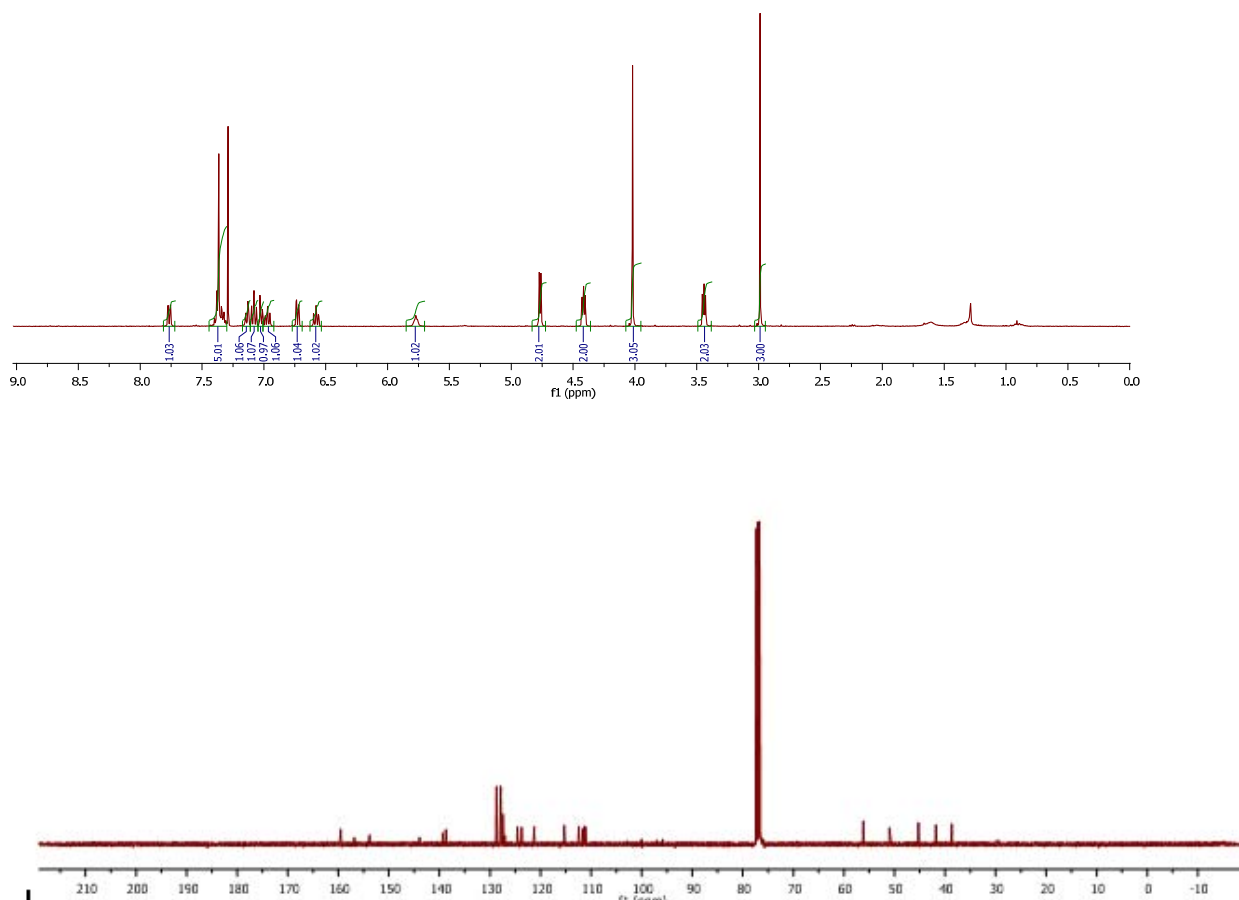


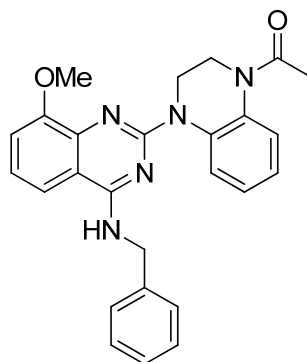


KSC-25-17

***N*-Benzyl-8-methoxy-2-(4-methyl-3,4-dihydroquinoxalin-1(2*H*)-yl)quinazolin-4-amine**

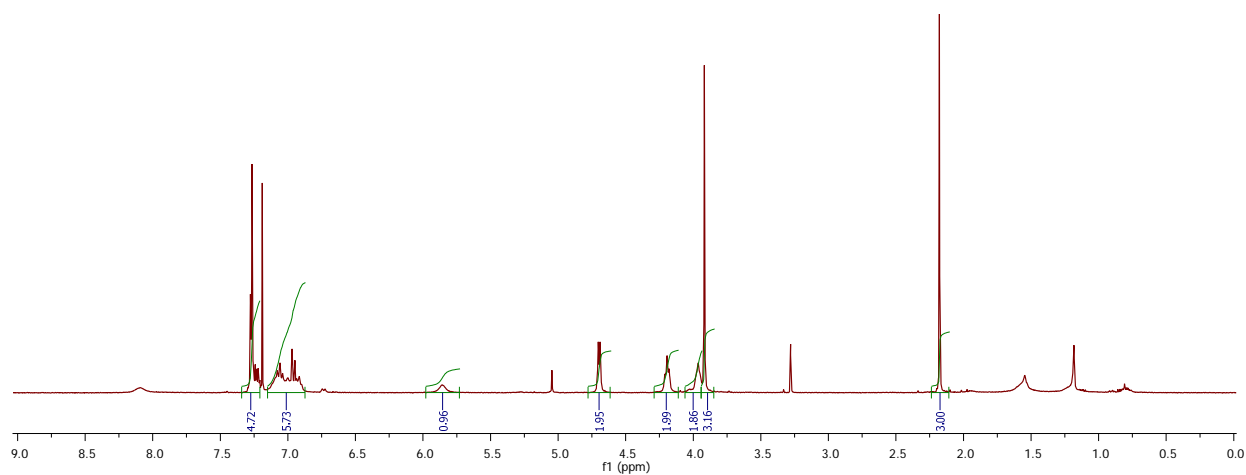
(S156). Yield: 10.0 mg, 73%. ^1H NMR (400 MHz, CDCl_3) δ 7.77 (dd, $J = 1.4, 8.1$ Hz, 1H), 7.44 – 7.30 (m, 5H), 7.14 (d, $J = 6.9$ Hz, 1H), 7.08 (t, $J = 7.9$ Hz, 1H), 7.05 – 7.01 (m, 1H), 6.96 (dd, $J = 4.2, 11.2$ Hz, 1H), 6.73 (dd, $J = 1.3, 8.2$ Hz, 1H), 6.58 (t, $J = 7.6$ Hz, 1H), 5.77 (s, 1H), 4.77 (d, $J = 5.4$ Hz, 2H), 4.47 – 4.36 (m, 2H), 4.02 (s, 3H), 3.49 – 3.38 (m, 2H), 2.99 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.5, 156.8, 153.8, 143.9, 139.4, 138.7, 128.7, 127.9, 127.5, 127.1, 124.6, 123.7, 121.2, 115.3, 112.4, 111.7, 111.3, 111.1, 56.2, 51.0, 45.3, 41.8, 38.7. HRMS (m/z): calcd for $\text{C}_{25}\text{H}_{26}\text{N}_5\text{O}$ ($M+H$) 412.2137; found 412.2148.

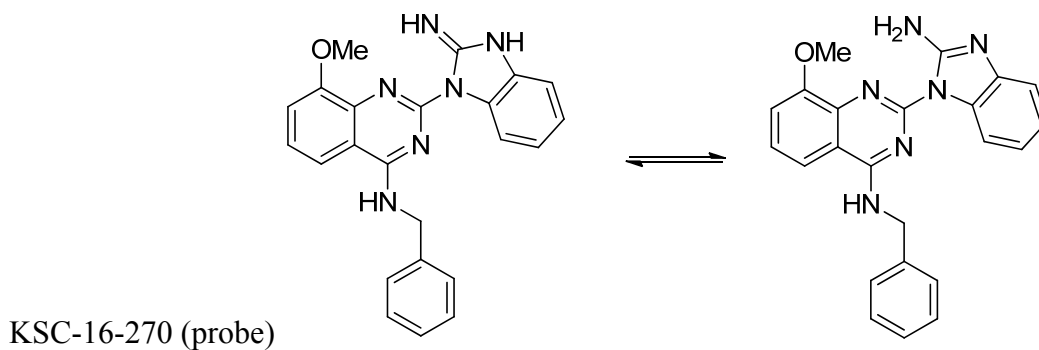




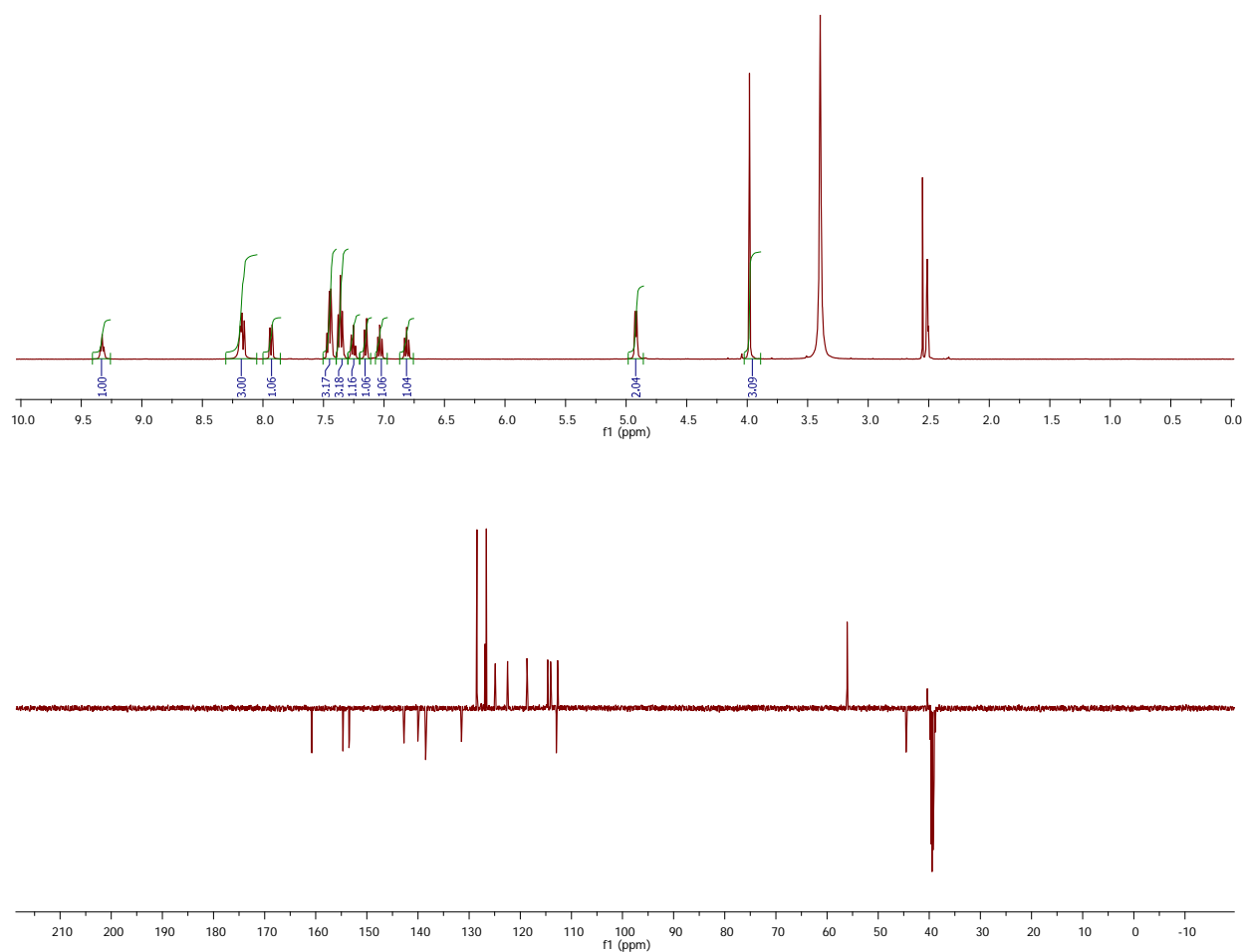
KSC-25-15c1

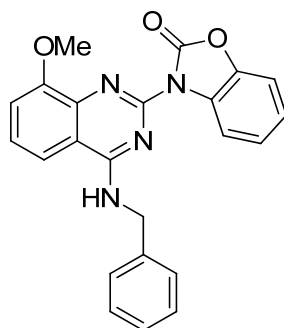
1-(4-(4-(Benzylamino)-8-methoxyquinazolin-2-yl)-3,4-dihydroquinoxalin-1(2H)-yl)ethanone (S157). Yield: 8.2 mg, 37%. ^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.21 (m, 5H), 7.15 – 6.87 (m, 6H), 5.98 – 5.73 (m, 1H), 4.70 (d, $J = 5.4$ Hz, 2H), 4.19 (s, br. 2H), 3.96 (s, br. 2H), 3.92 (s, 3H), 2.18 (s, 3H). HRMS (m/z): calcd for $\text{C}_{26}\text{H}_{26}\text{N}_5\text{O}_2$ ($\text{M}+\text{H}$) 440.2087; found 440.2096.





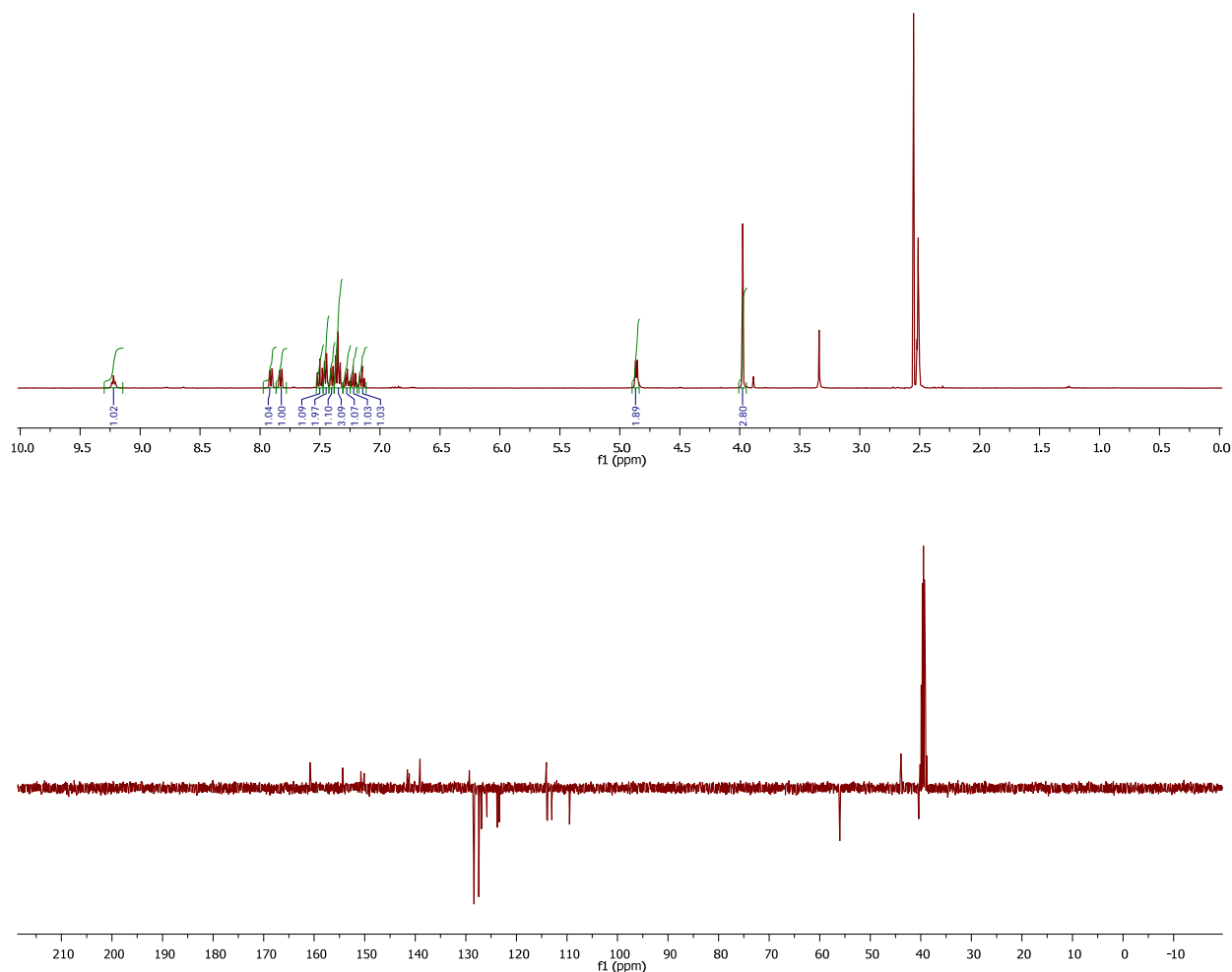
2-(2-Amino-1*H*-benzo[*d*]imidazol-1-yl)-*N*-benzyl-8-methoxyquinazolin-4-amine (S158 or ML240). Yield: 14.6 mg, 55%. ¹H NMR (400 MHz, DMSO) δ 9.33 (t, J = 5.9 Hz, 1H), 8.31 – 8.05 (m, 3H), 7.93 (d, J = 7.5 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.39 – 7.30 (m, 3H), 7.25 (t, J = 7.3 Hz, 1H), 7.15 (d, J = 7.1 Hz, 1H), 7.03 (td, J = 1.2, 7.6 Hz, 1H), 6.87 – 6.76 (m, 1H), 4.92 (d, J = 5.8 Hz, 2H), 3.98 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 160.8, 154.7, 153.5, 153.4, 142.8, 140.0, 138.5, 131.5, 128.5, 126.9, 126.6, 124.9, 122.5, 118.7, 114.8, 114.6, 114.1, 113.0, 112.7, 56.1, 44.5. HRMS (m/z): calcd for C₂₃H₂₁N₆O (M+H) 397.1777; found 397.1776.

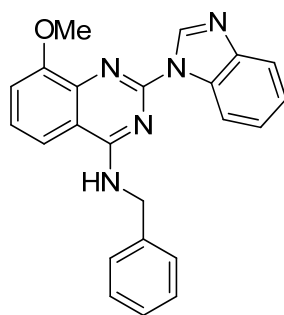




KSC-16-262

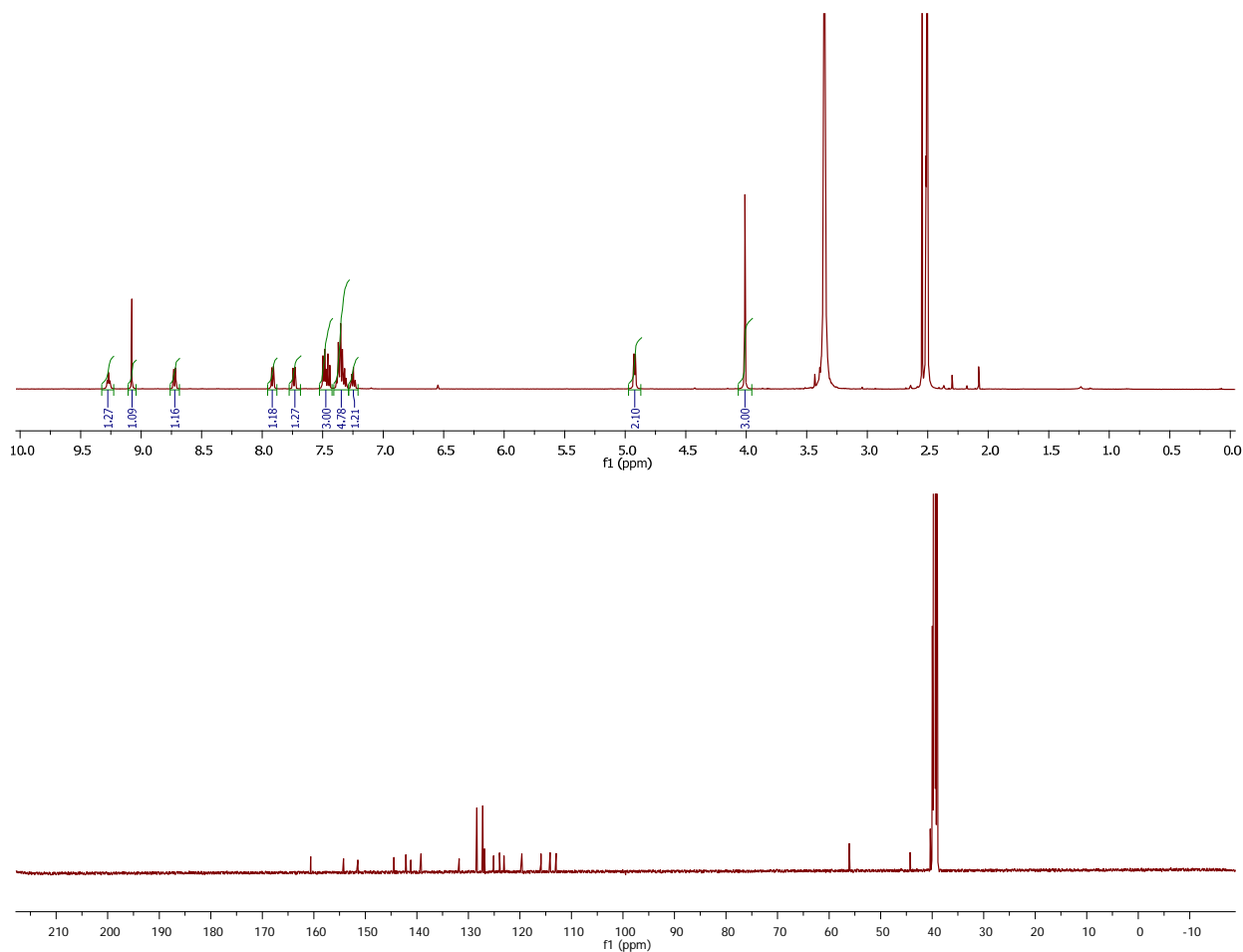
3-(4-(Benzylamino)-8-methoxyquinazolin-2-yl)benzo[d]oxazol-2(3H)-one (S159). Yield: 6.6 mg, 25%. ^1H NMR (400 MHz, DMSO) δ 9.22 (t, J = 6.0 Hz, 1H), 7.91 (d, J = 7.4 Hz, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.50 (t, J = 8.1 Hz, 1H), 7.45 (d, J = 7.0 Hz, 2H), 7.40 (d, J = 7.9 Hz, 1H), 7.38 – 7.31 (m, 3H), 7.27 (t, J = 7.3 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 7.15 (t, J = 7.8 Hz, 1H), 4.86 (d, J = 5.9 Hz, 2H), 3.98 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.8, 154.3, 150.7, 150.1, 141.6, 141.2, 139.1, 129.3, 128.4, 127.4, 126.9, 125.8, 123.8, 123.4, 114.1, 114.0, 113.8, 113.0, 109.5, 56.0, 43.9. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{19}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) 399.1457; found 399.1451.

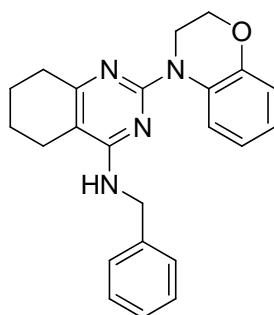




KSC-25-3

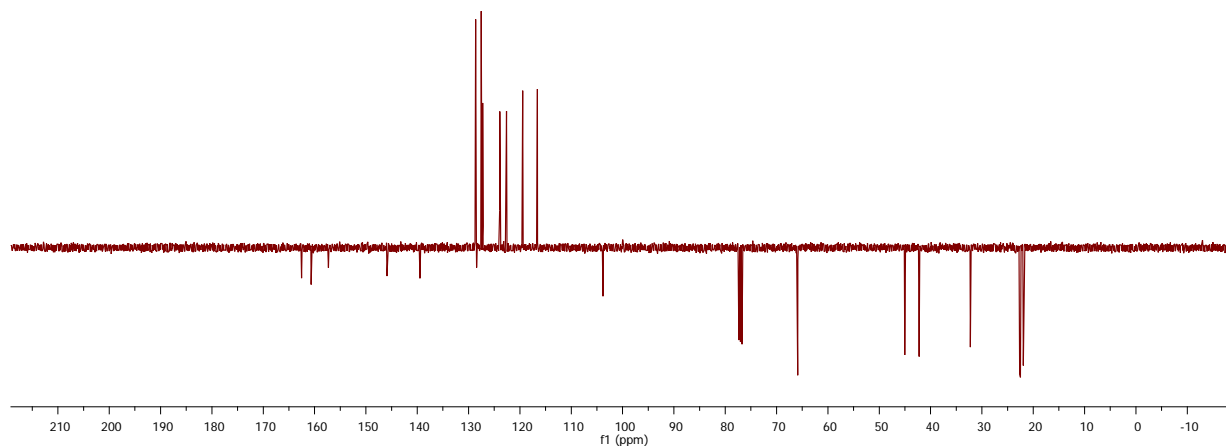
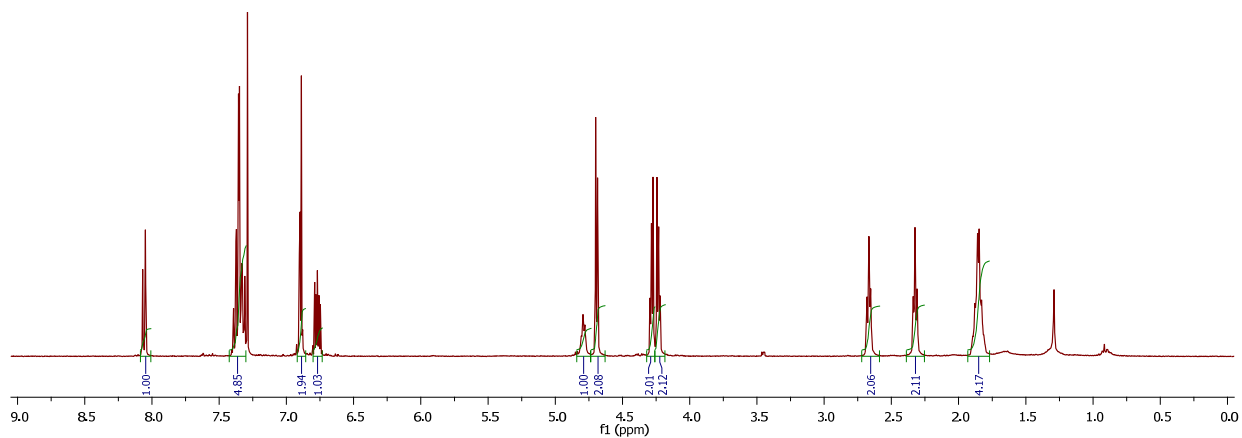
2-(1H-Benzo[d]imidazol-1-yl)-N-benzyl-8-methoxyquinazolin-4-amine (S160). Yield: 3.7 mg, 19%. ^1H NMR (500 MHz, DMSO) δ 9.27 (s, 1H), 9.08 (s, 1H), 8.72 (d, $J = 7.5$ Hz, 1H), 7.91 (d, $J = 7.4$ Hz, 1H), 7.74 (d, $J = 7.4$ Hz, 1H), 7.53 – 7.42 (m, 3H), 7.39 – 7.30 (m, 5H), 7.25 (d, $J = 7.4$ Hz, 1H), 4.92 (d, $J = 5.8$ Hz, 2H), 4.01 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 160.6, 154.3, 151.5, 144.5, 142.1, 141.2, 139.2, 131.8, 128.4, 127.2, 126.9, 125.1, 124.0, 123.1, 119.6, 115.9, 114.14, 114.12, 113.0, 56.1, 44.3. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{20}\text{N}_5\text{O}$ ($M+H$) 382.1668; found 382.1658.

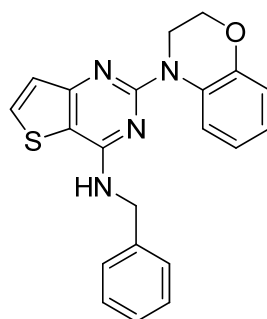




KSC-16-290

2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-5,6,7,8-tetrahydroquinazolin-4-amine (ML241). Yield: 9.0 mg, 66%. ^1H NMR (400 MHz, CDCl_3) δ 8.09 – 8.01 (m, 1H), 7.42 – 7.30 (m, 5H), 6.92 – 6.86 (m, 2H), 6.80 – 6.73 (m, 1H), 4.79 (s, 1H), 4.69 (d, $J = 5.6$ Hz, 2H), 4.28 (dd, $J = 3.1, 5.0$ Hz, 2H), 4.23 (dd, $J = 3.1, 5.0$ Hz, 2H), 2.67 (t, $J = 5.7$ Hz, 2H), 2.32 (t, $J = 5.7$ Hz, 2H), 1.93 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.5, 160.7, 157.3, 145.9, 139.5, 128.6, 128.5, 127.5, 127.3, 123.9, 122.6, 119.5, 116.6, 103.8, 65.9, 45.0, 42.2, 32.2, 22.6, 22.5, 21.9. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{25}\text{N}_4\text{O}$ ($M+H$) 373.2028; found 373.2030.

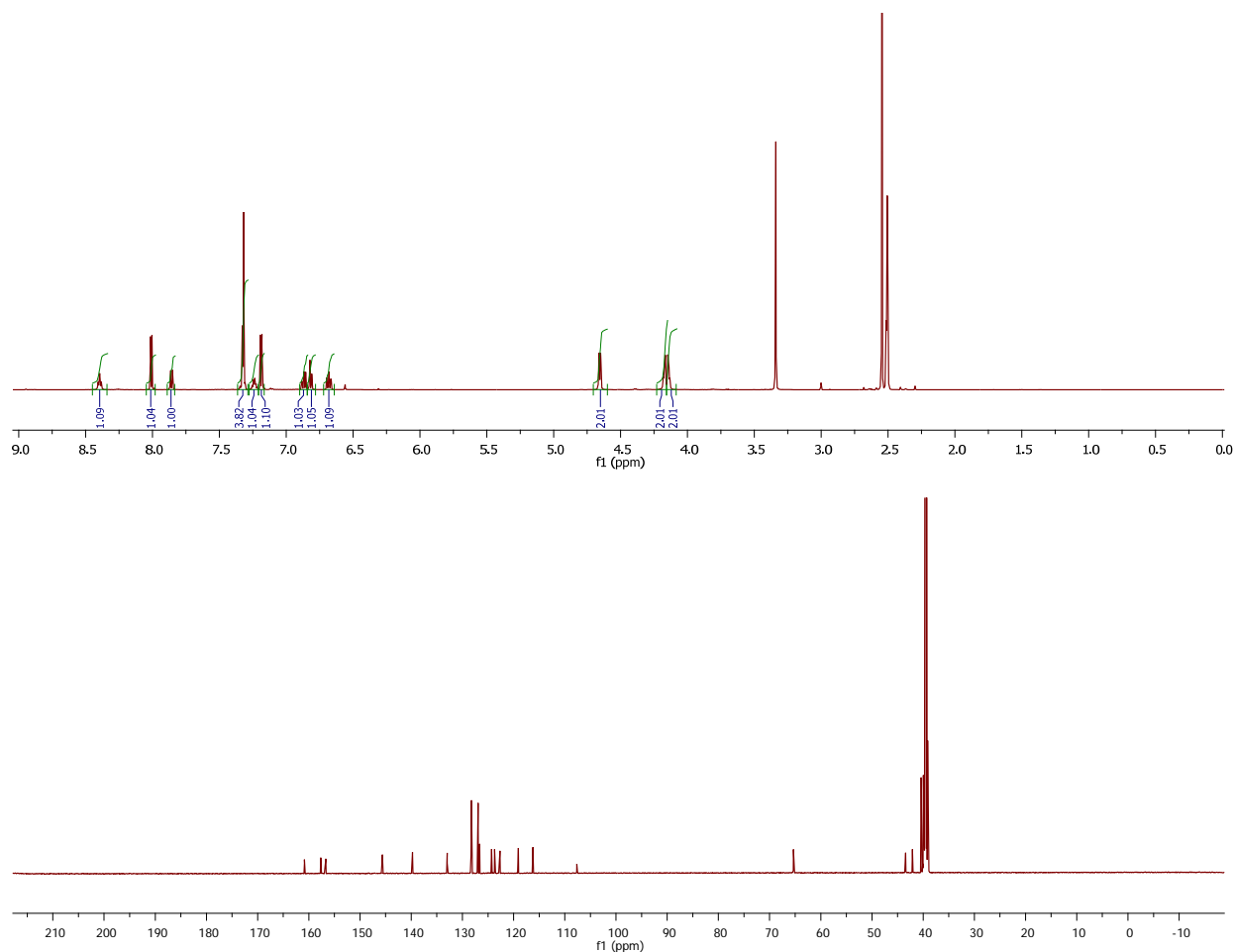


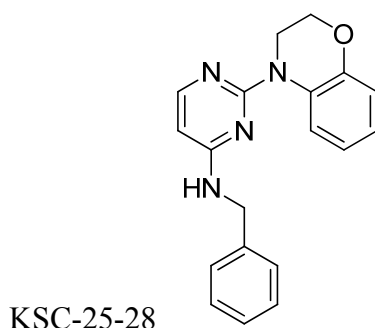


KSC-25-14

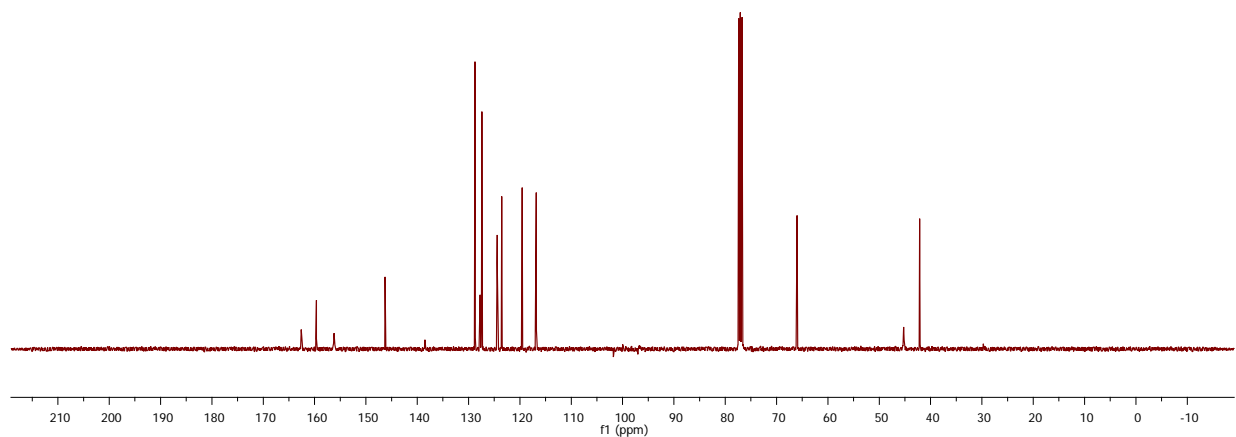
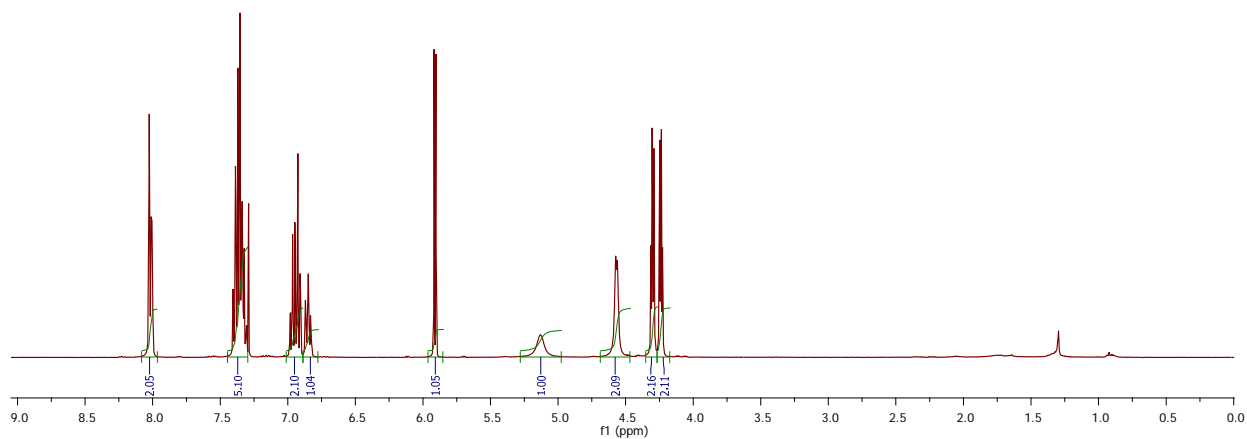
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzylthieno[3,2-*d*]pyrimidin-4-amine (S162 or 17).

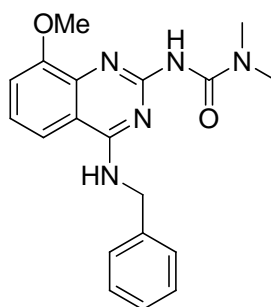
Yield: 8.2 mg, 41%. ^1H NMR (500 MHz, DMSO) δ 8.39 (t, $J = 5.9$ Hz, 1H), 8.01 (d, $J = 5.3$ Hz, 1H), 7.86 (dd, $J = 1.5, 8.3$ Hz, 1H), 7.36 – 7.29 (m, 4H), 7.28 – 7.21 (m, 1H), 7.19 (d, $J = 5.3$ Hz, 1H), 6.90 – 6.84 (m, 1H), 6.82 (dd, $J = 1.7, 8.1$ Hz, 1H), 6.68 (ddd, $J = 1.7, 7.1, 8.6$ Hz, 1H), 4.66 (d, $J = 5.9$ Hz, 2H), 4.23 – 4.16 (m, 2H), 4.15 – 4.13 (m, 2H). ^{13}C NMR (126 MHz, DMSO) δ 160.9, 157.7, 156.7, 145.6, 139.7, 133.0, 128.3, 128.2, 127.0, 126.6, 124.3, 123.7, 122.7, 119.1, 116.2, 107.6, 65.3, 43.4, 42.1. HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{19}\text{N}_4\text{OS}$ ($\text{M}+\text{H}$) 375.1280; found 375.1284.





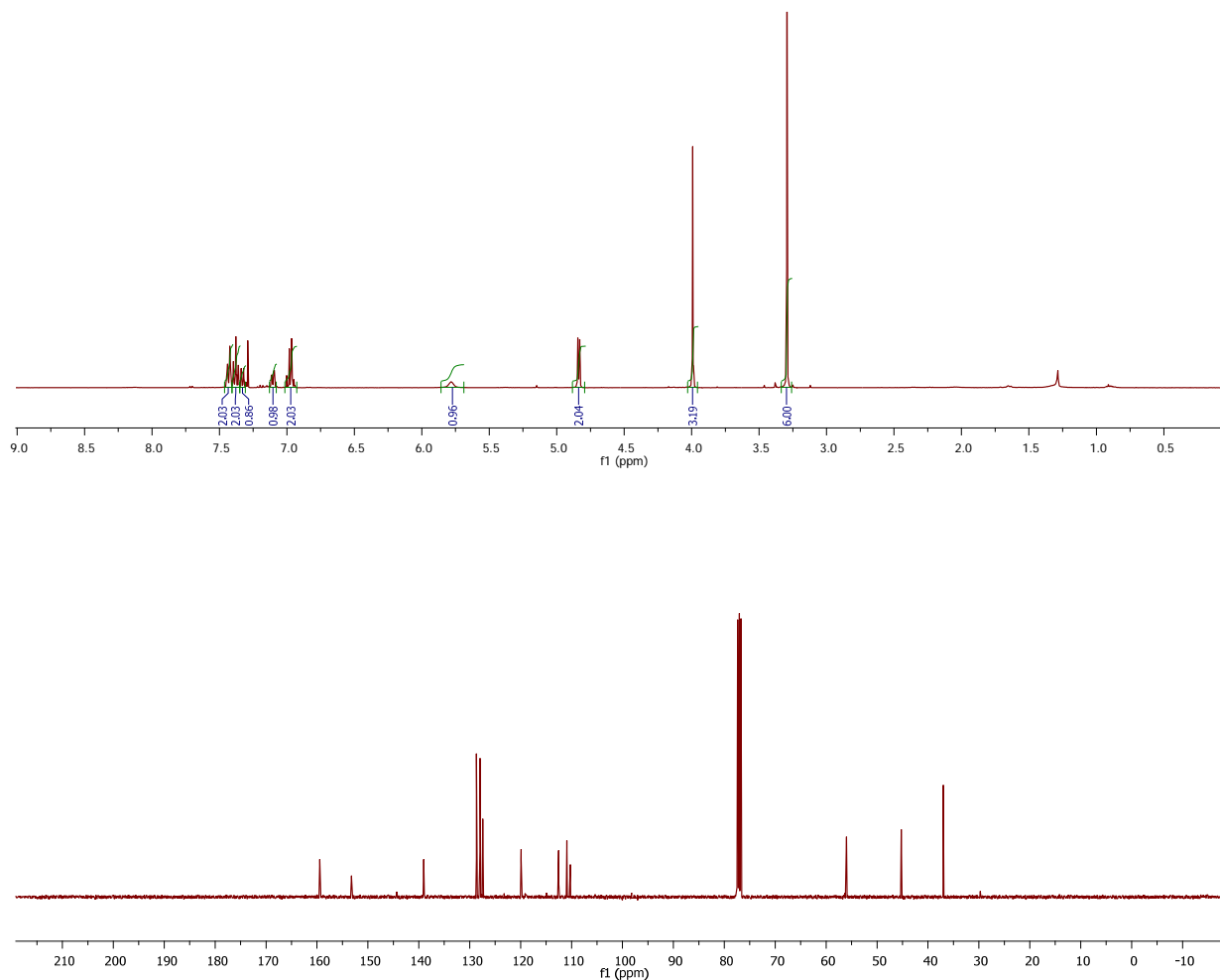
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-benzylpyrimidin-4-amine (S165 or 32). Yield: 20.0 mg, 69%. ^1H NMR (400 MHz, CDCl_3) δ 8.08 – 7.96 (m, 2H), 7.45 – 7.30 (m, 5H), 7.01 – 6.89 (m, 2H), 6.89 – 6.78 (m, 1H), 5.91 (d, $J = 5.8$ Hz, 1H), 5.13 (s, 1H), 4.57 (d, $J = 5.0$ Hz, 2H), 4.35 – 4.27 (m, 2H), 4.27 – 4.17 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.6, 159.7, 156.2, 146.3, 138.5, 128.7, 127.8, 127.5, 127.4, 124.4, 123.6, 119.6, 116.8, 66.0, 45.3, 42.1. HRMS (m/z): calcd for $\text{C}_{19}\text{H}_{19}\text{N}_4\text{O}$ ($M+H$) 319.1559; found 319.1555.

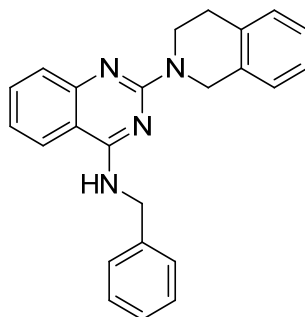




KSC-25-19

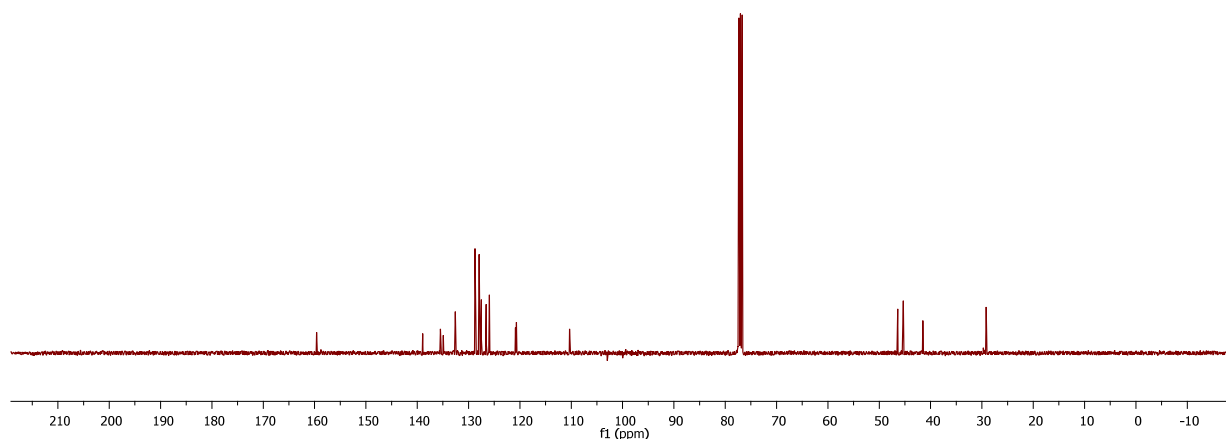
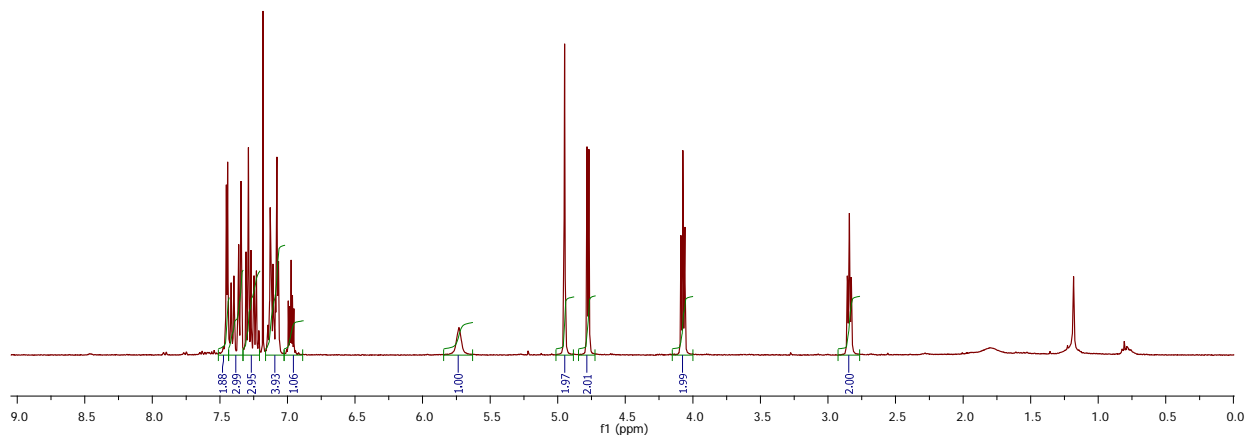
3-(4-(Benzylamino)-8-methoxyquinazolin-2-yl)-1,1-dimethylurea (S169). Yield: 12.3 mg, 70%. ^1H NMR (400 MHz, CDCl_3) δ 7.46 – 7.41 (m, 2H), 7.41 – 7.35 (m, 2H), 7.33 (dt, $J = 2.2$, 5.6 Hz, 1H), 7.10 (dd, $J = 2.2$, 7.2 Hz, 1H), 7.01 – 6.93 (m, 2H), 5.78 (s, 1H), 4.84 (d, $J = 5.4$ Hz, 2H), 3.99 (s, 3H), 3.29 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.5, 159.3, 153.2, 144.3, 139.0, 128.7, 128.0, 127.4, 119.9, 112.5, 110.9, 110.2, 56.0, 45.2, 37.0. HRMS not detected because the product was not stable under LC conditions.

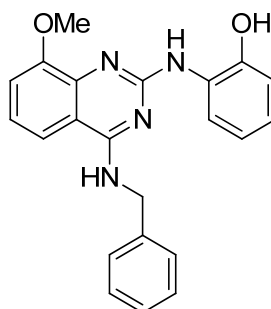




KSC-16-187

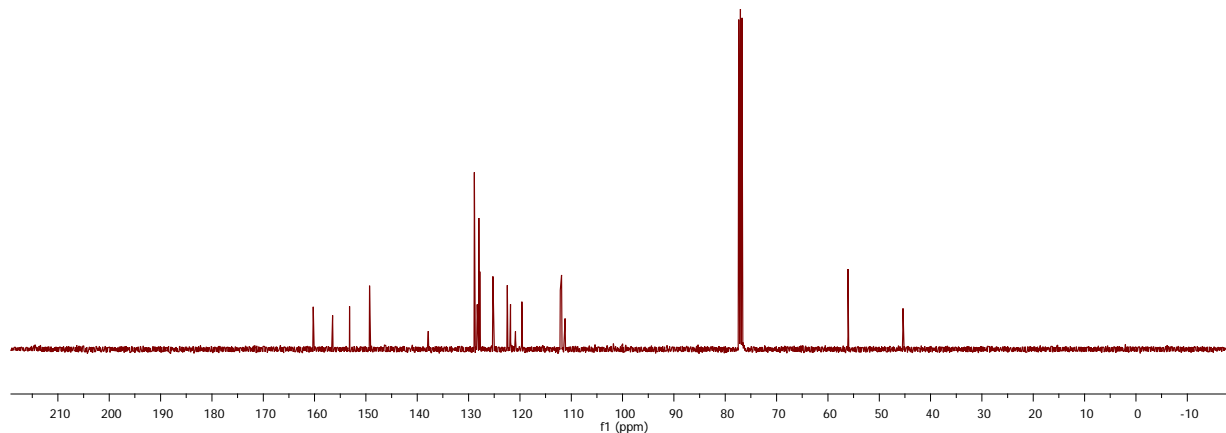
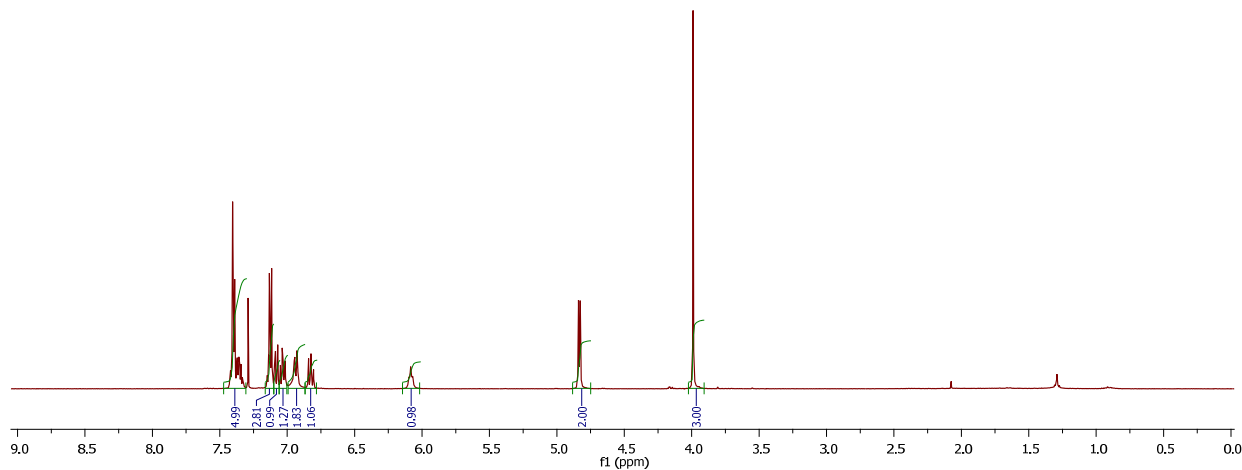
***N*-Benzyl-2-(3,4-dihydroisoquinolin-2(*1H*)-yl)quinazolin-4-amine (S170 or 20).** Yield: 8.0 mg, 59%. ^1H NMR (400 MHz, CDCl_3) δ 7.45 (d, $J = 3.6$ Hz, 2H), 7.41 (d, $J = 8.2$ Hz, 1H), 7.35 (d, $J = 7.3$ Hz, 2H), 7.33 – 7.21 (m, 3H), 7.16 – 7.03 (m, 4H), 7.03 – 6.89 (m, 1H), 5.73 (s, br. 1H), 4.95 (s, 2H), 4.78 (d, $J = 5.4$ Hz, 2H), 4.07 (t, $J = 5.9$ Hz, 2H), 2.84 (t, $J = 5.9$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.6, 139.0, 135.5, 134.9, 132.6, 128.7, 128.6, 127.9, 127.5, 126.6, 126.03, 125.95, 120.9, 120.7, 110.3, 46.4, 45.3, 41.5, 29.2. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4$ ($M+H$) 367.1923; found 367.1921.

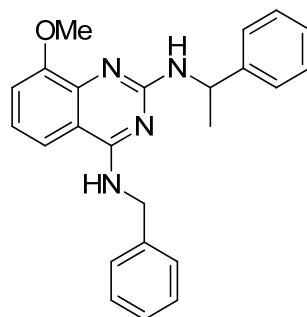




KSC-16-203

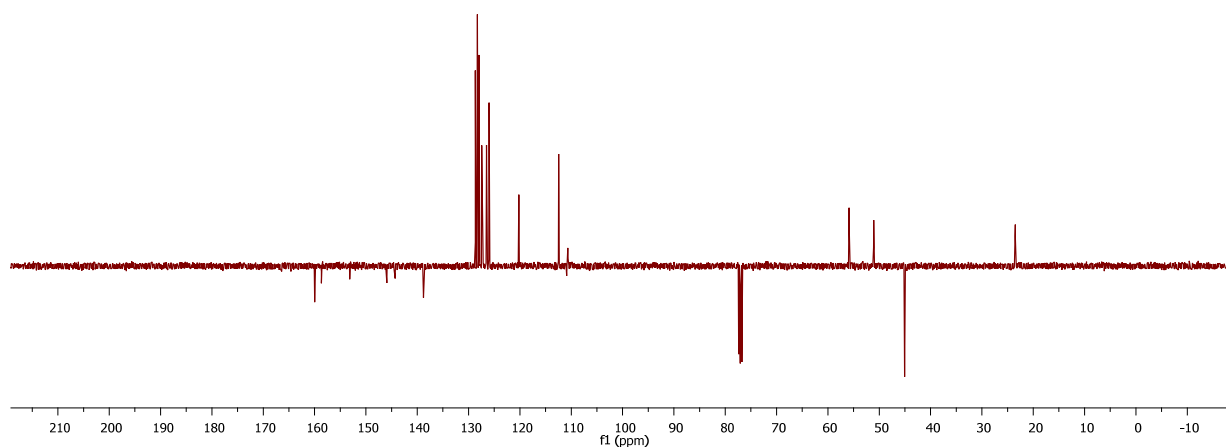
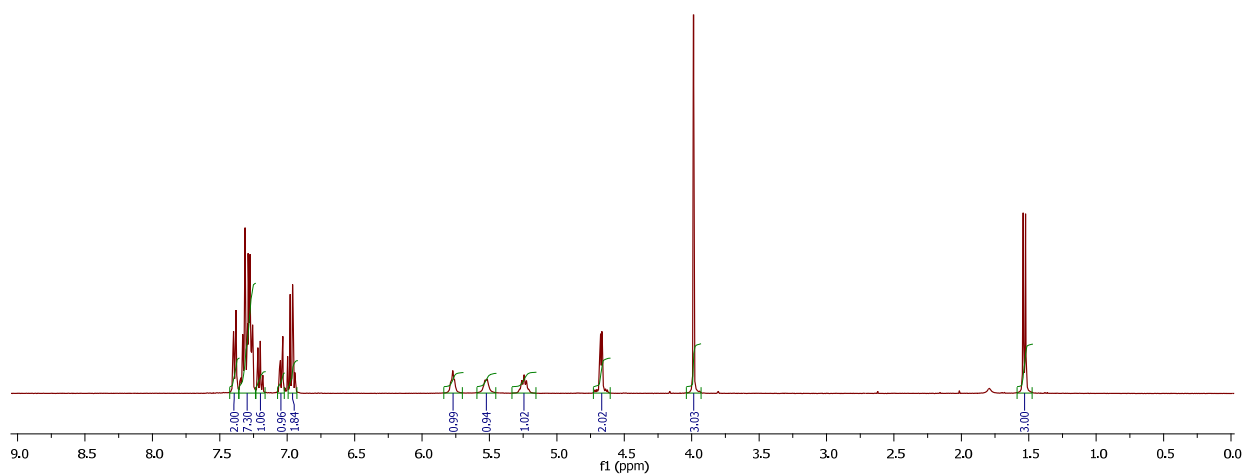
2-((4-(Benzylamino)-8-methoxyquinazolin-2-yl)amino)phenol (S171). Yield: 21.3 mg, 86%. ^1H NMR (400 MHz, CDCl_3) δ 7.47 – 7.31 (m, 5H), 7.16 – 7.10 (m, 3H), 7.10 – 7.06 (m, 1H), 7.03 (td, $J = 2.0, 6.8$ Hz, 1H), 6.94 (d, $J = 6.6$ Hz, 2H), 6.87 – 6.78 (m, 1H), 6.08 (s, br. 1H), 4.83 (d, $J = 5.4$ Hz, 2H), 3.99 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 160.3, 156.5, 153.2, 149.3, 137.9, 128.9, 128.3, 128.0, 127.8, 125.3, 122.5, 121.8, 120.9, 119.6, 112.1, 111.9, 111.2, 56.1, 45.4. HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{21}\text{N}_4\text{O}_2$ ($M+H$) 373.1665; found 373.1657.

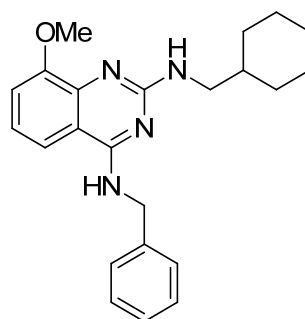




KSC-16-273

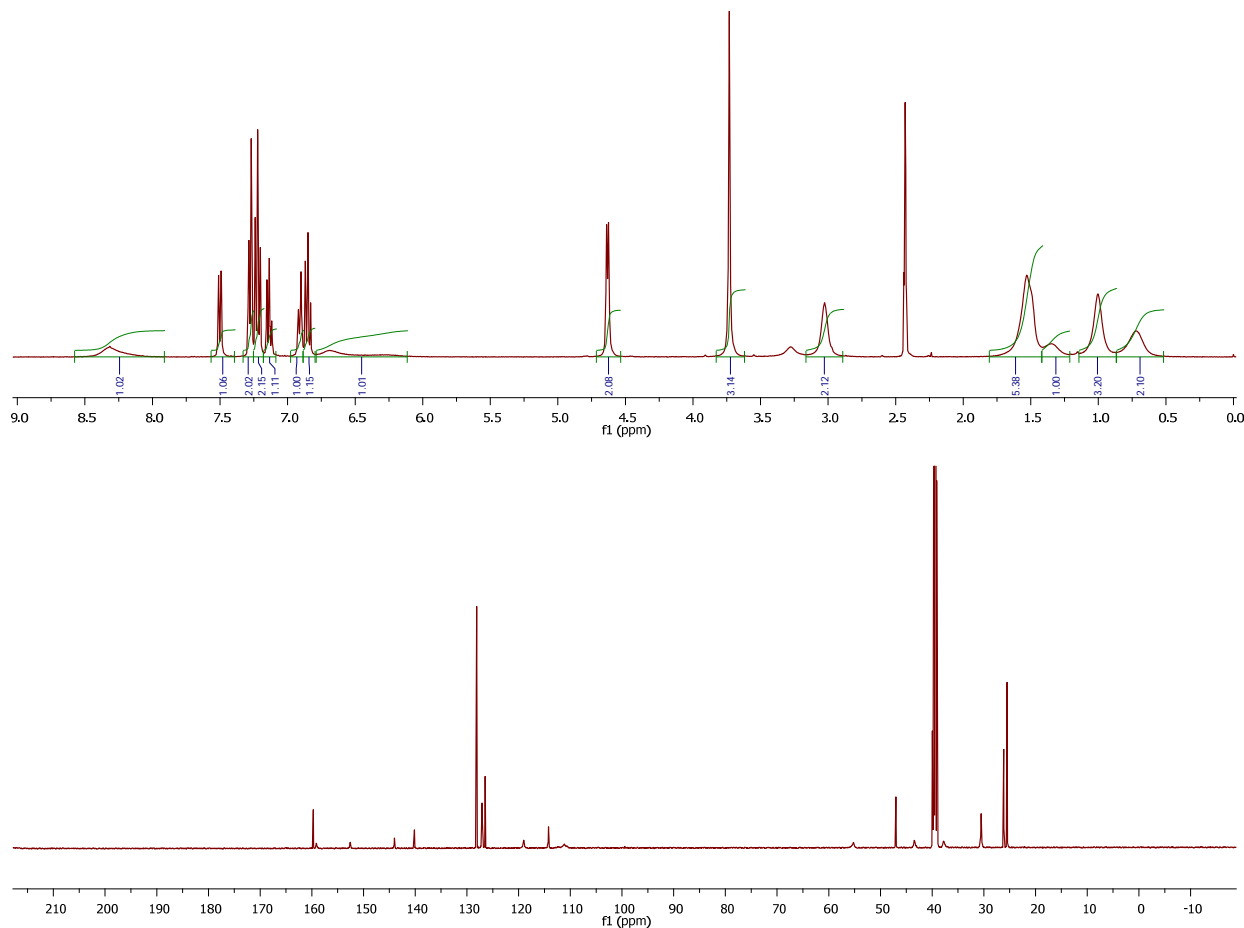
***N*⁴-Benzyl-8-methoxy-*N*²-(1-phenylethyl)quinazoline-2,4-diamine (S172).** Yield: 20.5 mg, 80%. ¹H NMR (400 MHz, CDCl₃) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.36 – 7.24 (m, 7H), 7.23 – 7.16 (m, 1H), 7.04 (dd, *J* = 2.2, 7.4 Hz, 1H), 6.96 (td, *J* = 4.3, 7.5 Hz, 2H), 5.77 (s, 1H), 5.52 (s, 1H), 5.33 – 5.16 (m, 1H), 4.69 (dd, *J* = 9.4, 11.0 Hz, 2H), 3.99 (s, 3H), 1.53 (d, *J* = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 158.7, 153.1, 145.9, 144.3, 138.8, 128.7, 128.3, 128.0, 127.4, 126.5, 126.0, 120.2, 112.5, 110.9, 110.7, 55.9, 51.1, 45.1, 23.5. HRMS (*m/z*): calcd for C₂₄H₂₅N₄O (*M*+*H*) 385.2028; found 385.2018.

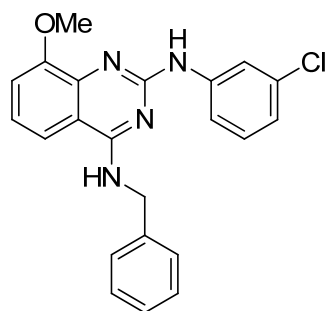




KSC-16-278

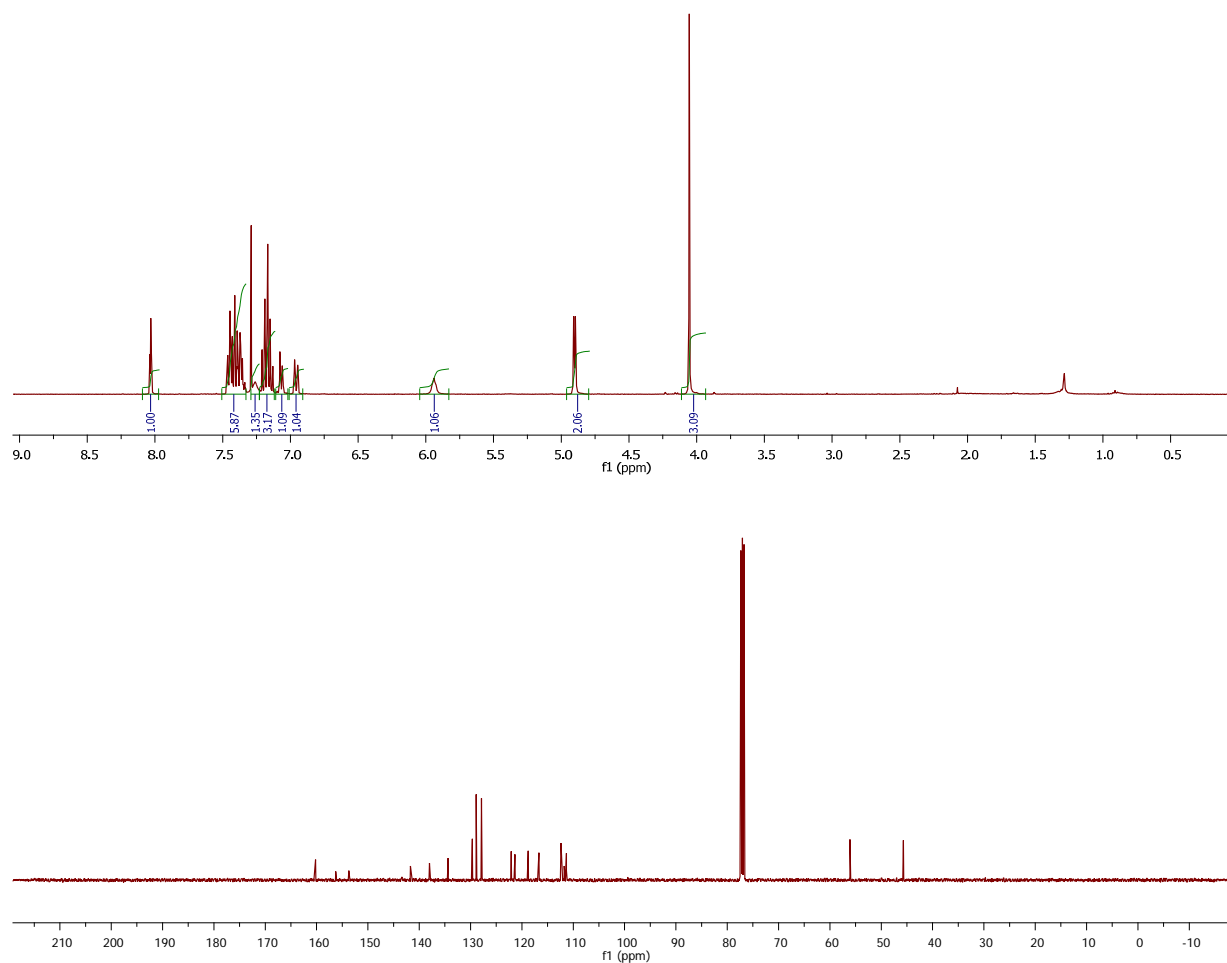
***N*⁴-Benzyl-*N*²-(cyclohexylmethyl)-8-methoxyquinazoline-2,4-diamine (S173).** Yield: 19.5 mg, 78%. ¹H NMR (400 MHz, DMSO) δ 8.58 – 7.91 (m, 1H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.28 (d, *J* = 7.1 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.14 (t, *J* = 7.2 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 6.85 (t, *J* = 7.9 Hz, 1H), 6.79 – 6.12 (m, 1H), 4.63 (d, *J* = 5.7 Hz, 2H), 3.73 (s, 3H), 3.02 (s, 2H), 1.53 (s, br. 5H), 1.42 – 1.21 (m, 1H), 1.00 (s, br., 3H), 0.72 (s, br., 2H). ¹³C NMR (101 MHz, DMSO) δ 159.8, 159.1, 152.6, 144.1, 140.2, 128.1, 127.1, 126.5, 119.0, 114.3, 111.0, 55.2, 47.0, 43.5, 37.8, 30.5, 26.2, 25.5. HRMS (*m/z*): calcd for C₂₃H₂₉N₄O (*M*+*H*) 377.2341; found 377.2338.

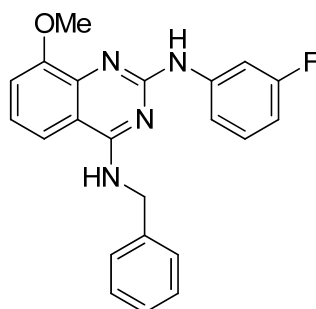




KSC-16-193

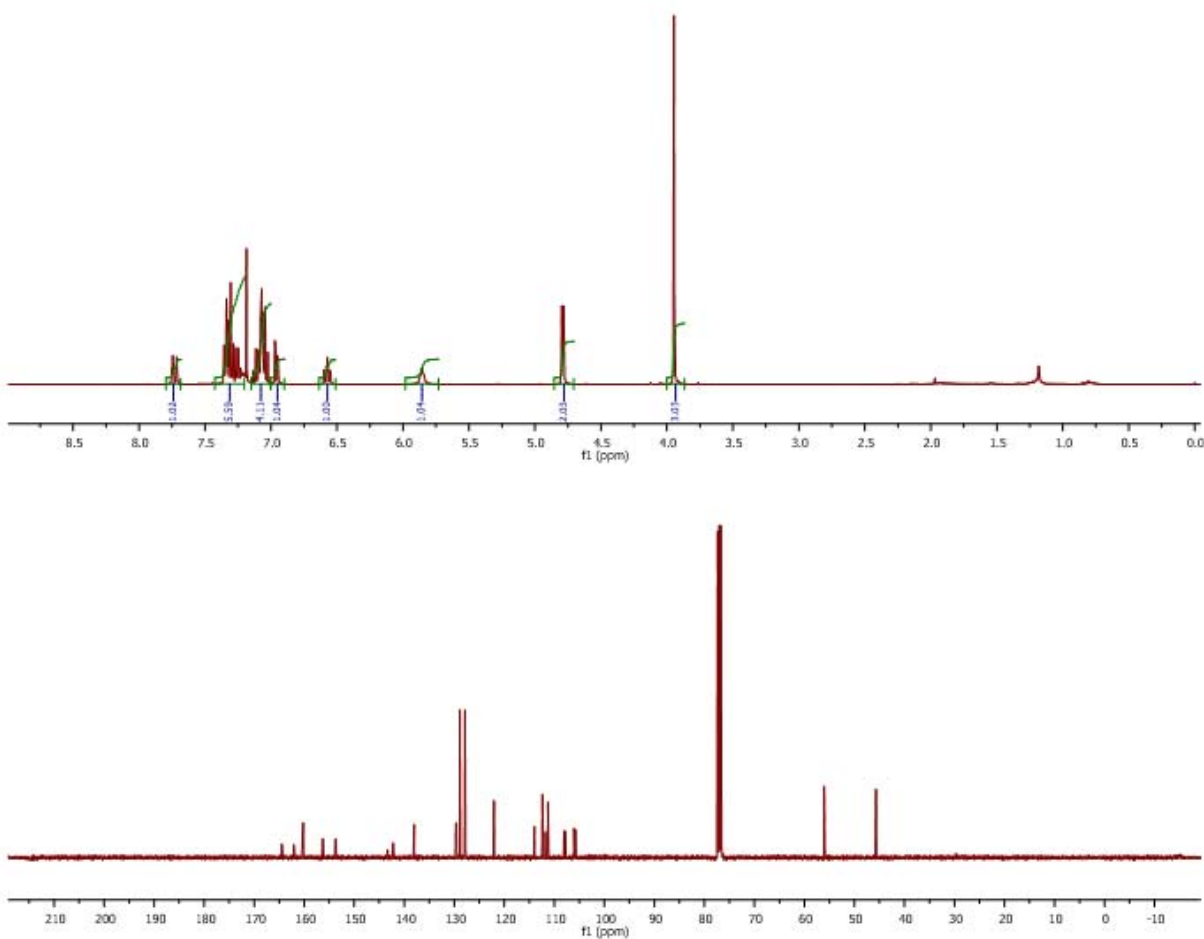
***N*⁴-Benzyl-*N*²-(3-chlorophenyl)-8-methoxyquinazoline-2,4-diamine (S174 or 50).** Yield: 9.6 mg, 74%. ¹H NMR (400 MHz, CDCl₃) δ 8.03 (t, *J* = 2.1 Hz, 1H), 7.51 – 7.33 (m, 6H), 7.28 (d, *J* = 11.5 Hz, 1H), 7.23 – 7.12 (m, 3H), 7.07 (dd, *J* = 1.9, 7.1 Hz, 1H), 6.96 (ddd, *J* = 0.9, 2.0, 7.9 Hz, 1H), 5.94 (s, br. 1H), 4.90 (d, *J* = 5.1 Hz, 2H), 4.05 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.2, 156.3, 153.7, 141.7, 138.0, 134.4, 129.7, 128.9, 127.9, 127.8, 122.1, 121.4, 118.8, 116.7, 112.4, 111.8, 111.3, 56.1, 45.7. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄O (*M*+*H*) 391.1326; found 391.1325.

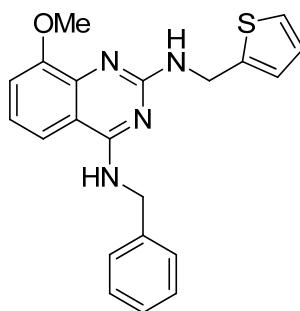




KSC-16-194

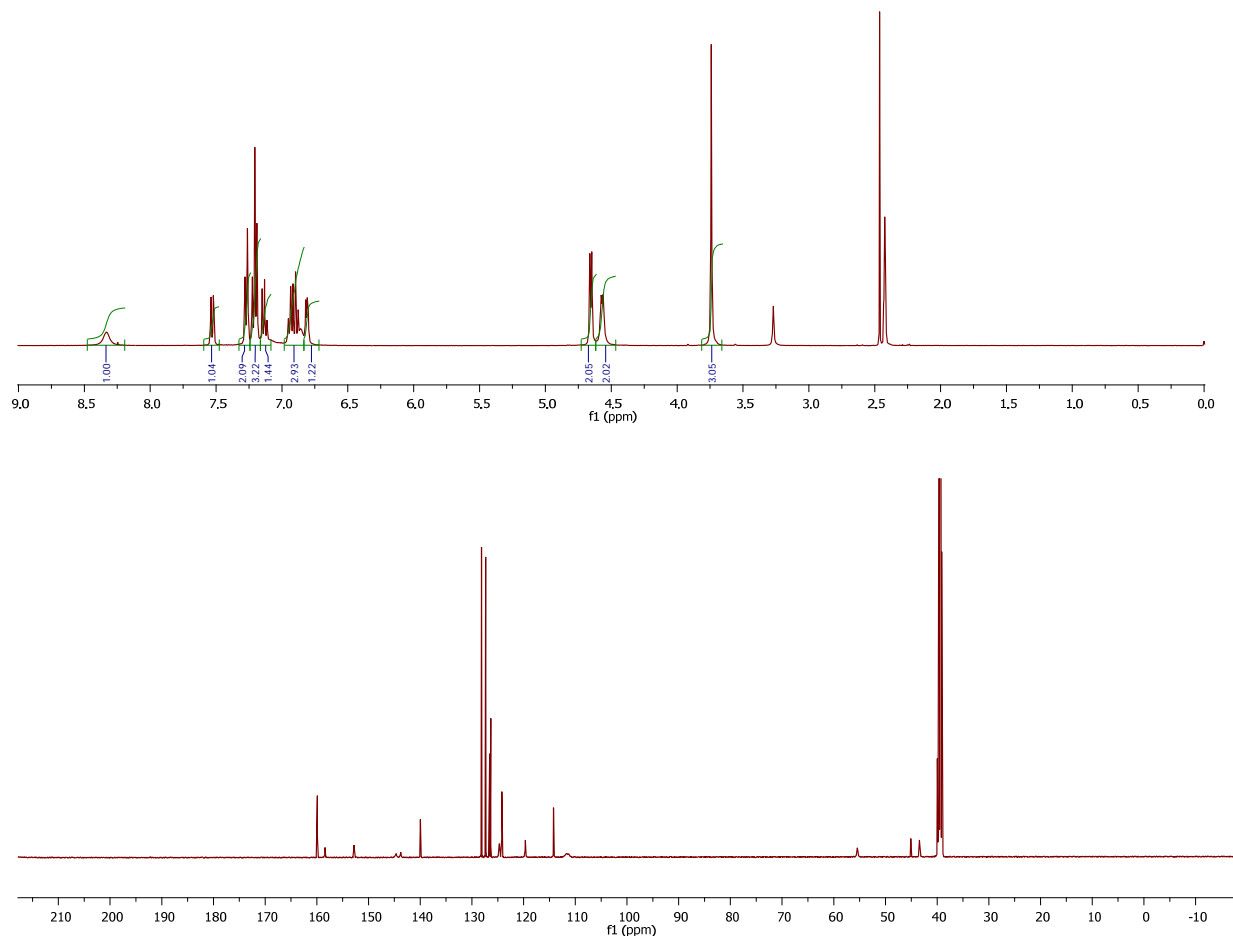
***N*⁴-Benzyl-*N*²-(3-fluorophenyl)-8-methoxyquinazoline-2,4-diamine (S175 or 51).** Yield: 12.2 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.73 (dt, *J* = 2.1, 11.8 Hz, 1H), 7.42 – 7.20 (m, 6H), 7.15 – 7.00 (m, 4H), 6.96 (dd, *J* = 1.7, 7.3 Hz, 1H), 6.64 – 6.51 (m, 1H), 5.86 (s, 1H), 4.79 (d, *J* = 5.1 Hz, 2H), 3.95 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 164.5, 162.1, 160.2, 156.3, 153.7, 143.3, 142.2, 142.1, 138.0, 129.7, 129.6, 128.9, 127.9, 127.8, 122.1, 114.0, 114.0, 112.4, 111.8, 111.3, 108.1, 107.8, 106.1, 105.8, 56.1, 45.7. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄O (*M*+*H*) 375.1621; found 375.1626.

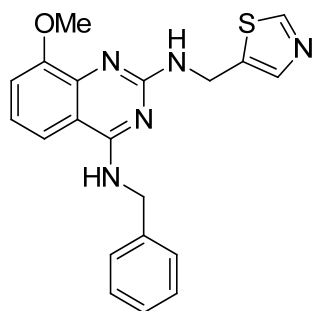




KSC-16-282

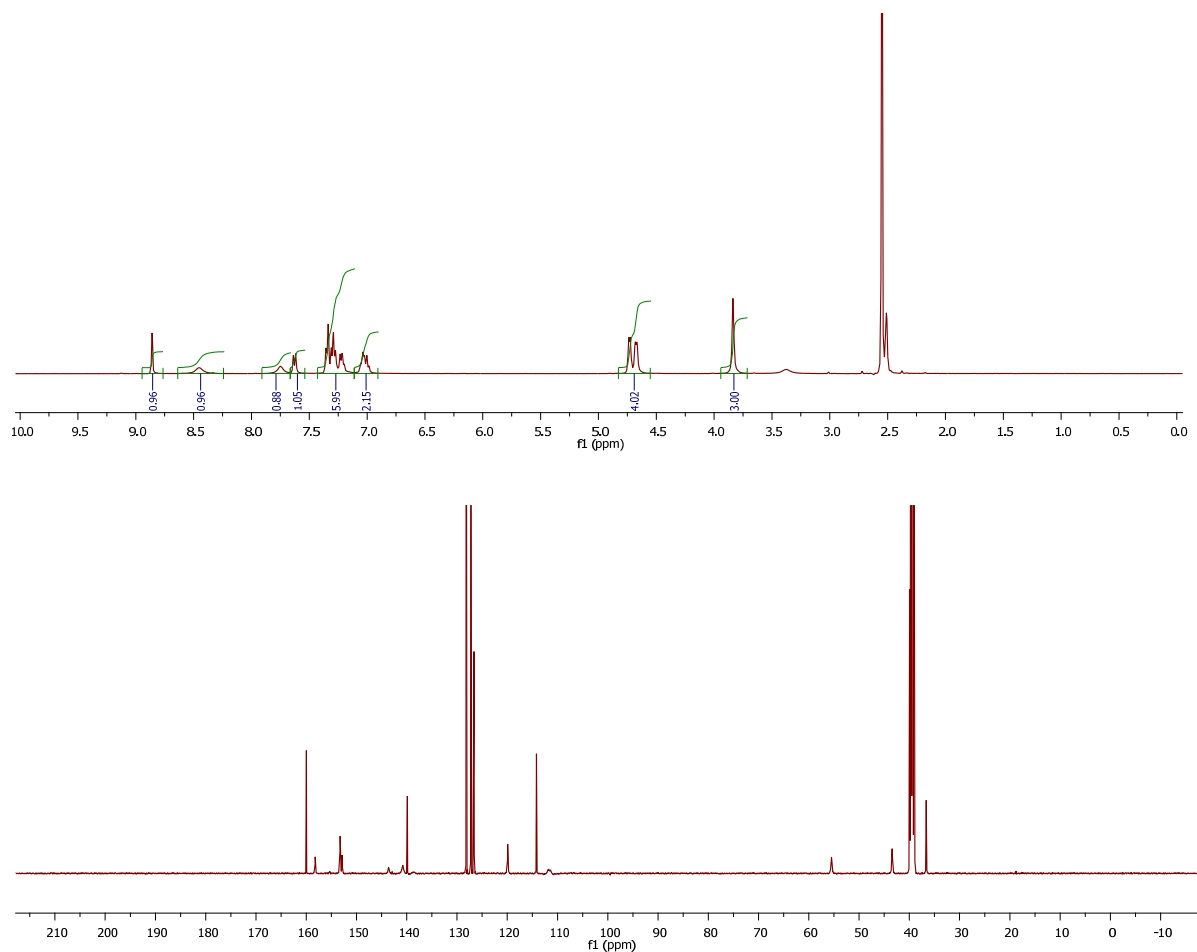
***N*⁴-Benzyl-8-methoxy-*N*²-(thiophen-2-ylmethyl)quinazoline-2,4-diamine (S176 or 52).** Yield: 17.9 mg, 71%. ¹H NMR (400 MHz, DMSO) δ 8.33 (s, 1H), 7.53 (dd, *J* = 1.3, 8.0 Hz, 1H), 7.27 (d, *J* = 7.2 Hz, 2H), 7.24 – 7.16 (m, 3H), 7.13 (dd, *J* = 6.0, 8.3 Hz, 1H), 6.98 – 6.83 (m, 3H), 6.83 – 6.72 (m, 1H), 4.66 (d, *J* = 5.8 Hz, 2H), 4.57 (d, *J* = 5.7 Hz, 2H), 3.74 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 159.9, 158.4, 152.8, 144.6, 143.8, 140.0, 128.2, 127.3, 126.6, 126.4, 124.7, 124.2, 119.7, 114.2, 111.7, 111.3, 55.4, 45.1, 43.4. HRMS (*m/z*): calcd for C₂₁H₂₁N₄OS (M+H) 377.1436; found 377.1433.

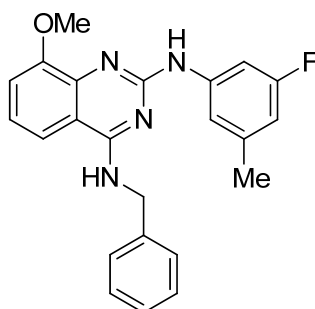




KSC-16-283

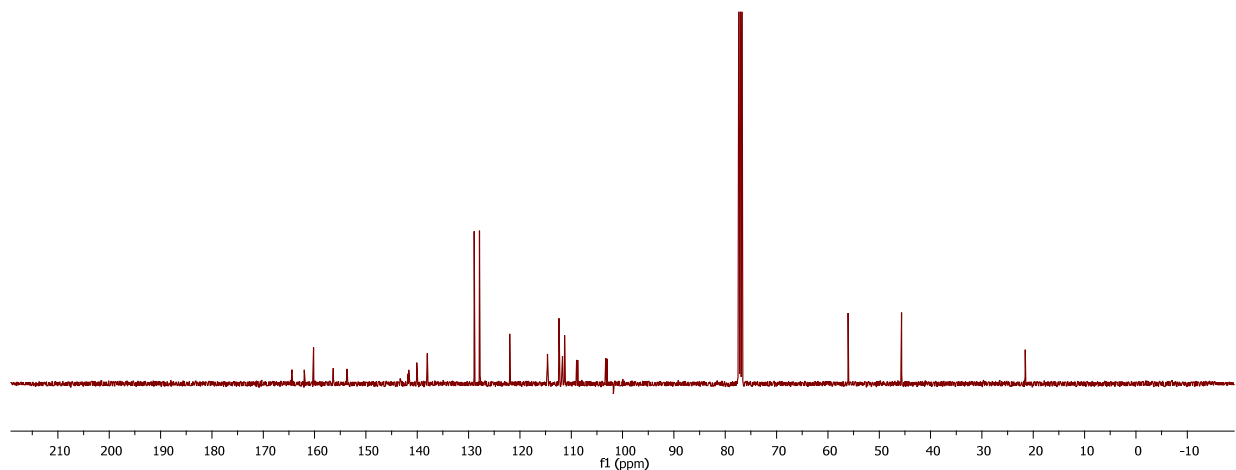
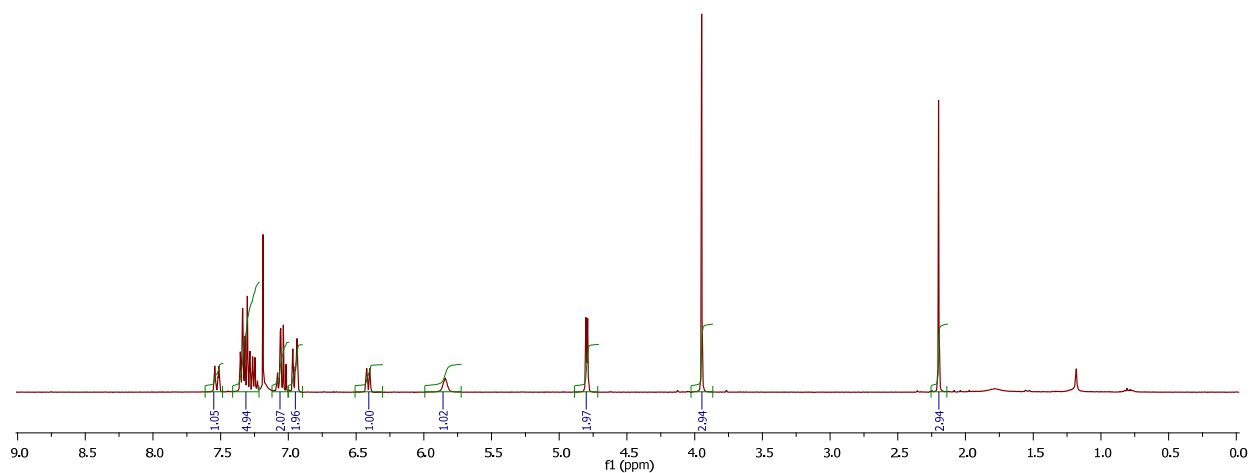
***N*⁴-Benzyl-8-methoxy-*N*²-(thiazol-5-ylmethyl)quinazoline-2,4-diamine (S177).** Yield: 18.7 mg, 74%. ¹H NMR (400 MHz, DMSO) δ 8.86 (s, 1H), 8.45 (s, 1H), 7.75 (s, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.43 – 7.11 (m, 6H), 7.02 (d, *J* = 13.8 Hz, 2H), 4.83 – 4.55 (m, 4H), 3.84 (s, 3H). ¹³C NMR (101 MHz, DMSO) δ 160.0, 158.2, 153.3, 152.9, 143.6, 140.8, 139.9, 128.2, 127.2, 126.6, 119.9, 114.2, 111.9, 111.4, 55.5, 43.4, 36.6. HRMS (*m/z*): calcd for C₂₀H₂₀N₅OS (*M*+*H*) 378.1389; found 378.1384.

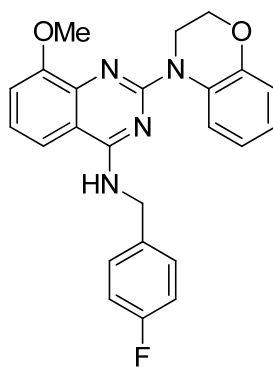




KSC-16-196

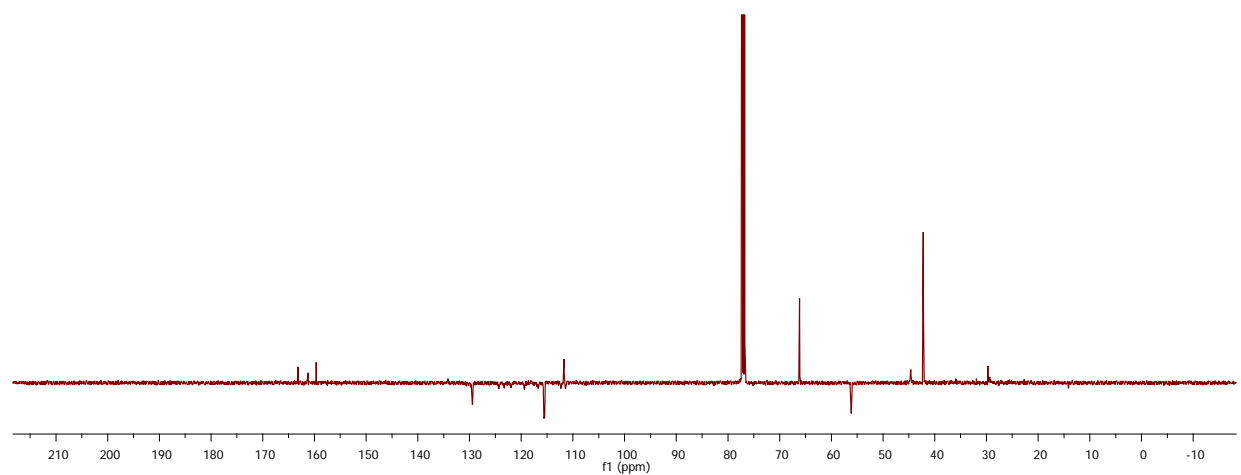
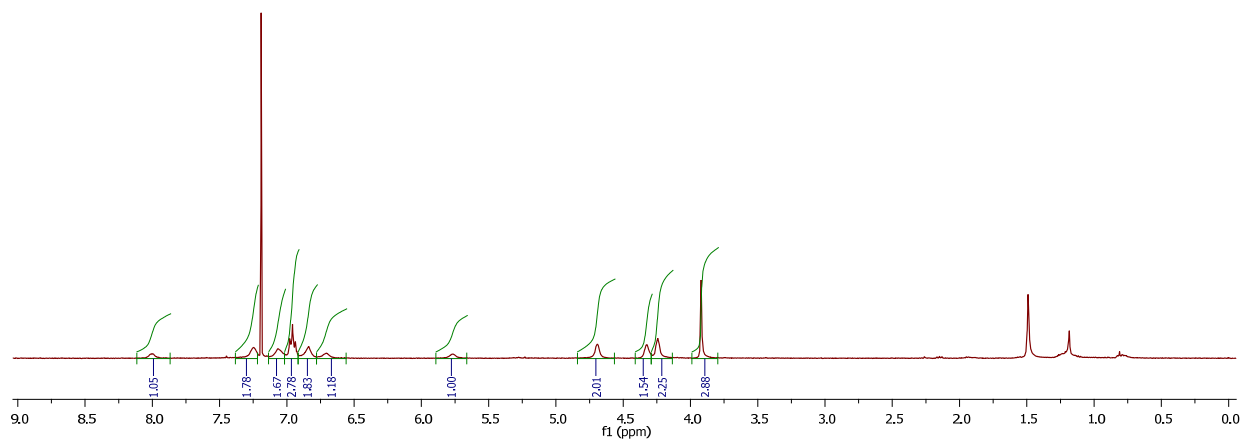
***N*⁴-Benzyl-*N*²-(3-fluoro-5-methylphenyl)-8-methoxyquinazoline-2,4-diamine (S178).** Yield: 11.1 mg, 86%. ¹H NMR (400 MHz, CDCl₃) δ 7.53 (d, *J* = 11.7 Hz, 1H), 7.41 – 7.22 (m, 5H), 7.12 – 7.00 (m, 2H), 7.00 – 6.89 (m, 2H), 6.41 (d, *J* = 9.3 Hz, 1H), 5.84 (s, 1H), 4.80 (d, *J* = 5.1 Hz, 2H), 3.95 (s, 3H), 2.20 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 164.4, 162.0, 160.2, 156.4, 153.7, 141.8, 141.7, 140.1, 140.0, 138.0, 128.9, 127.9, 127.8, 122.0, 114.6, 112.4, 111.7, 111.3, 109.0, 108.7, 103.3, 103.0, 56.1, 45.7, 21.58, 21.56. HRMS (*m/z*): calcd for C₂₃H₂₂FN₄O (*M*+*H*) 389.1778; found 389.1781.

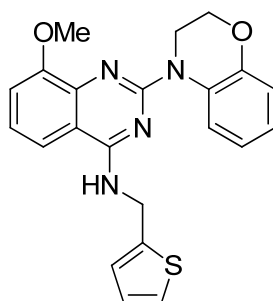




KSC-16-261

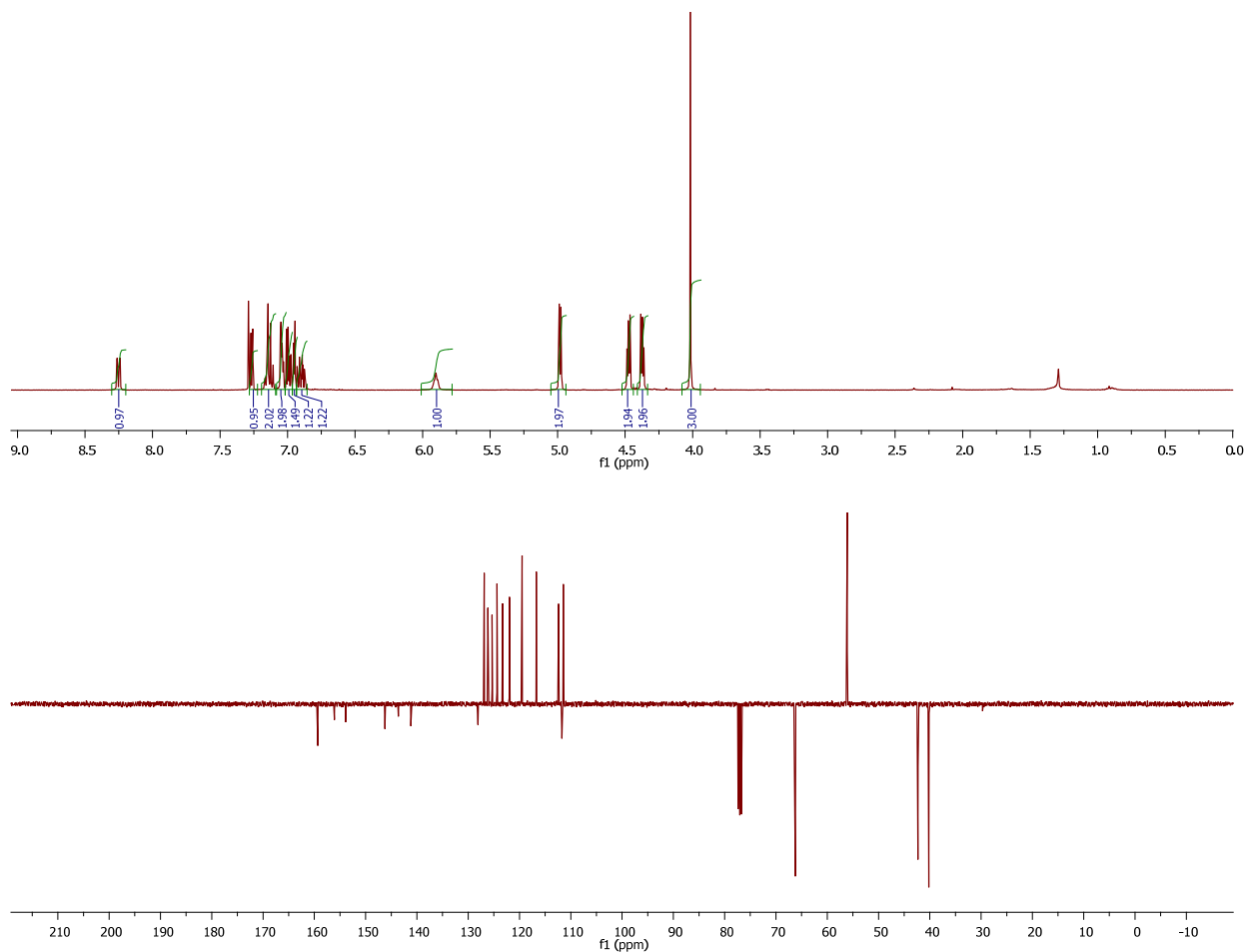
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-*N*-(4-fluorobenzyl)-8-methoxyquinazolin-4-amine (S179 or 40). Yield: 2.9 mg, 22%. ^1H NMR (400 MHz, CDCl_3) δ 8.12 – 7.87 (m, 1H), 7.25 (s, br. 2H), 7.14 – 7.02 (m, 2H), 6.98 – 6.93 (m, 2H), 6.84 (s, br. 2H), 6.78 – 6.56 (m, 1H), 5.89 – 5.66 (m, 1H), 4.69 (s, br. 2H), 4.32 (s, br. 2H), 4.24 (s, br. 2H), 3.92 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 163.2, 161.2, 159.7, 134.2, 129.5, 124.4, 123.3, 122.0, 119.4, 116.7, 115.6, 115.5, 112.3, 111.7, 111.4, 66.2, 56.2, 44.6, 42.2, 29.7. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{22}\text{FN}_4\text{O}_2$ ($\text{M}+\text{H}$) 417.1727; found 417.1726.

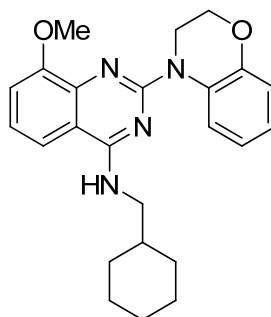




KSC-16-295

2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-8-methoxy-*N*-(thiophen-2-ylmethyl)quinazolin-4-amine (S180 or 41). Yield: 15.9 mg, 80%. ^1H NMR (400 MHz, CDCl_3) δ 8.25 (dd, $J = 1.4, 8.2$ Hz, 1H), 7.27 (dd, $J = 1.3, 5.1$ Hz, 1H), 7.19 – 7.09 (m, 2H), 7.08 – 7.02 (m, 2H), 6.99 (ddd, $J = 2.5, 4.1, 8.1$ Hz, 1H), 6.95 (dd, $J = 1.8, 4.0$ Hz, 1H), 6.93 – 6.86 (m, 1H), 5.90 (s, 1H), 4.98 (d, $J = 5.1$ Hz, 2H), 4.47 (dd, $J = 3.6, 5.3$ Hz, 2H), 4.37 (dd, $J = 3.6, 5.3$ Hz, 2H), 4.02 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.3, 156.1, 153.9, 146.2, 143.6, 141.2, 128.1, 126.9, 126.2, 125.4, 124.4, 123.3, 122.0, 119.5, 116.7, 112.4, 111.7, 111.5, 66.2, 56.1, 42.3, 40.2. HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{21}\text{N}_4\text{O}_2\text{S}$ ($M+H$) 405.1385; found 405.1383.

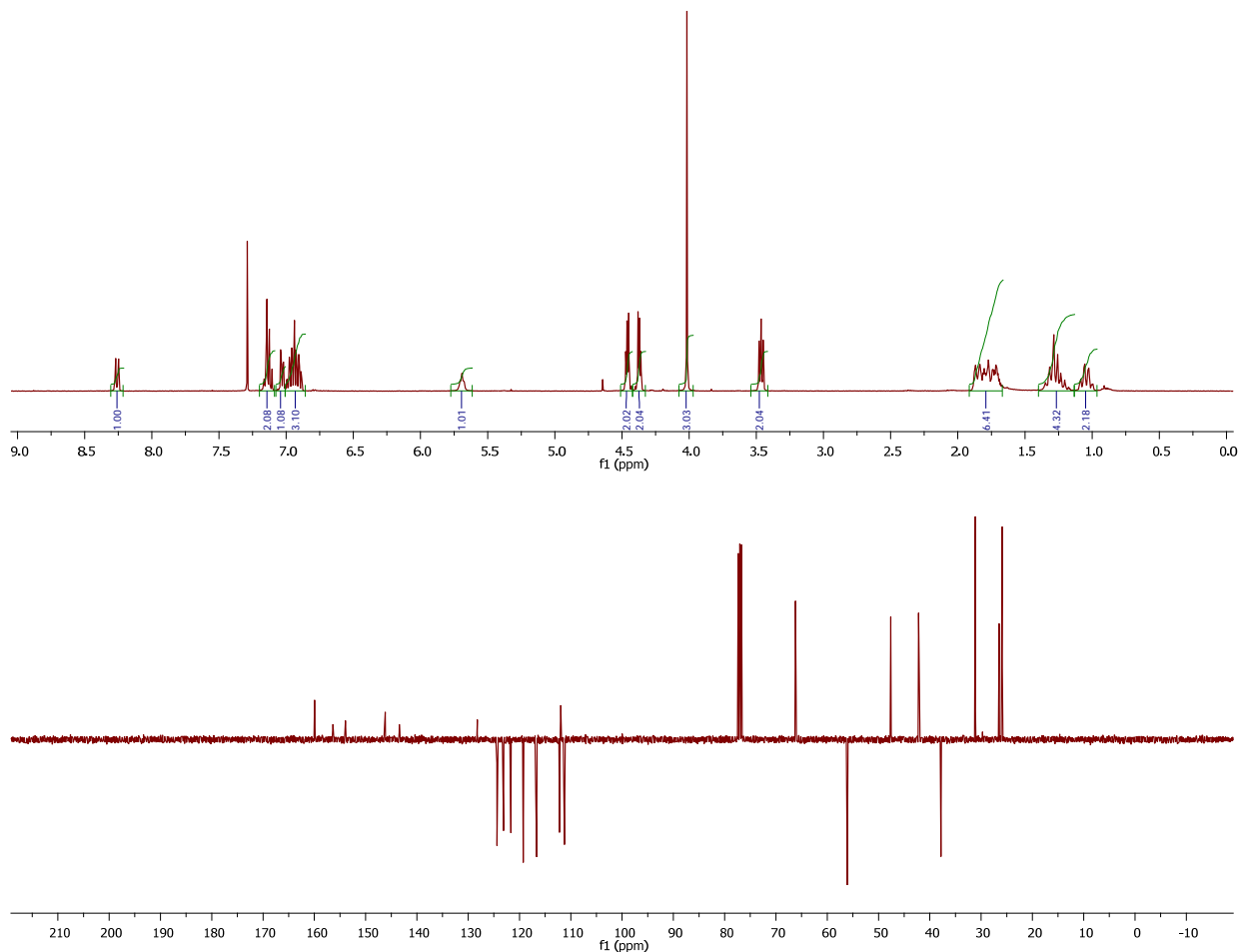


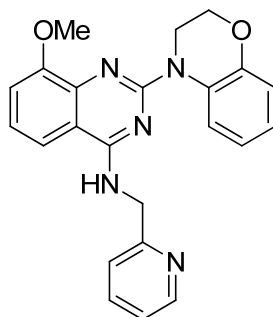


KSC-16-299

2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-(cyclohexylmethyl)-8-methoxyquinazolin-4-amine

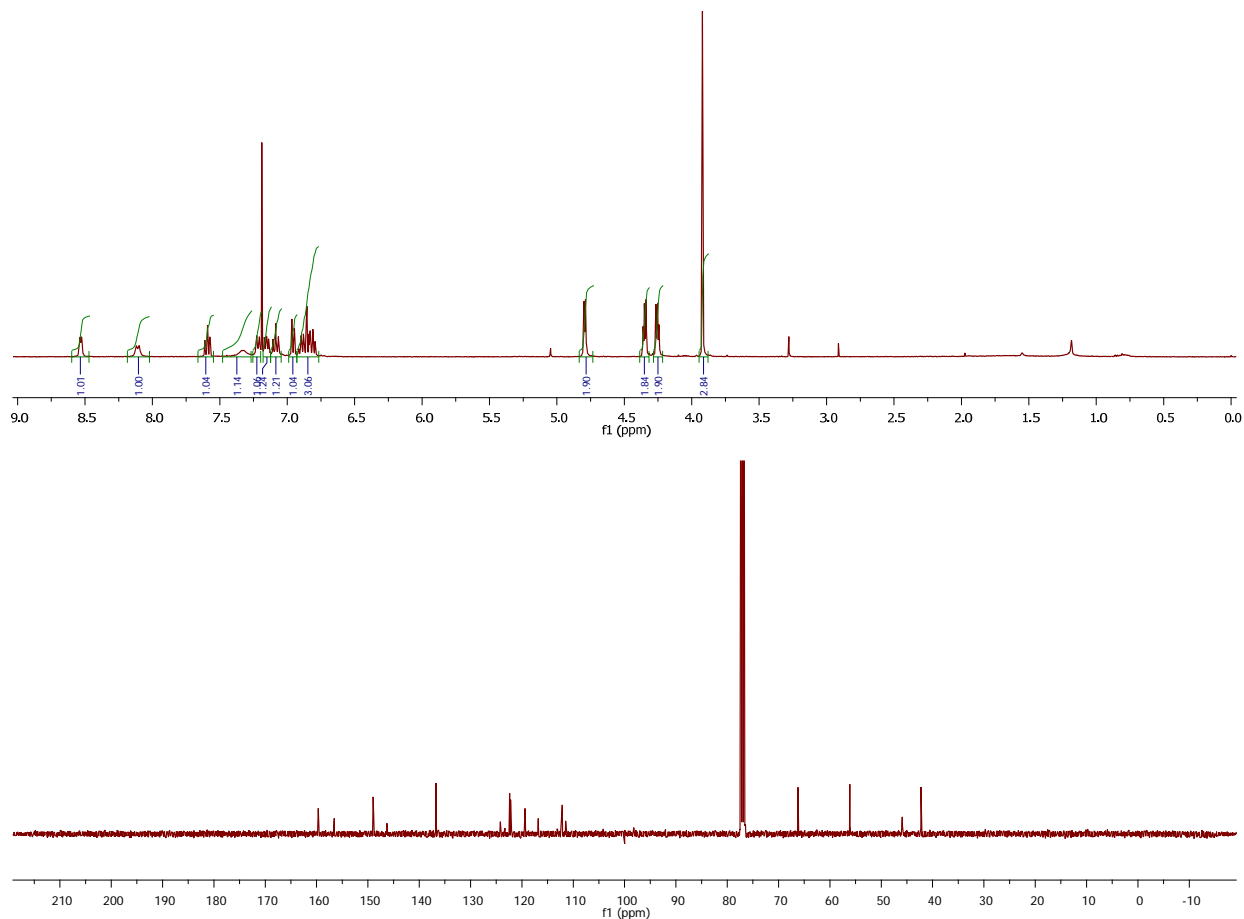
(S181 or 42). Yield: 13.6 mg, 69%. ^1H NMR (400 MHz, CDCl_3) δ 8.26 (dd, $J = 1.4, 8.1$ Hz, 1H), 7.20 – 7.09 (m, 2H), 7.03 (dd, $J = 1.9, 7.1$ Hz, 1H), 7.01 – 6.86 (m, 3H), 5.69 (s, 1H), 4.46 (dd, $J = 3.6, 5.2$ Hz, 2H), 4.37 (dd, $J = 3.6, 5.2$ Hz, 2H), 4.02 (s, 3H), 3.54 – 3.42 (m, 2H), 187 – 1.71 (m, 6H), 1.40 – 1.13 (m, 4H), 1.04 (q, $J = 12.0$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 160.0, 156.4, 153.9, 146.2, 143.4, 128.2, 124.4, 123.1, 121.7, 119.3, 116.7, 112.2, 111.9, 111.2, 66.2, 56.1, 47.6, 42.2, 37.8, 31.1, 26.5, 25.9. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{29}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) 405.2291; found 405.2289.

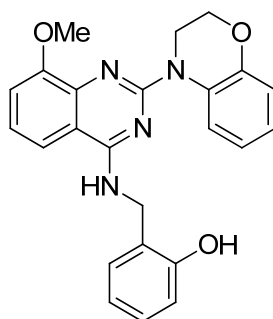




KSC-16-219

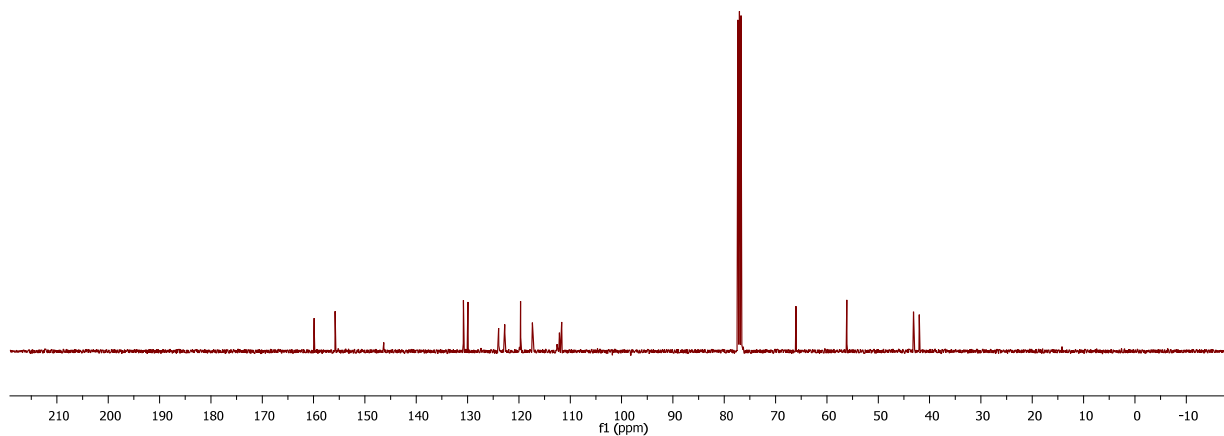
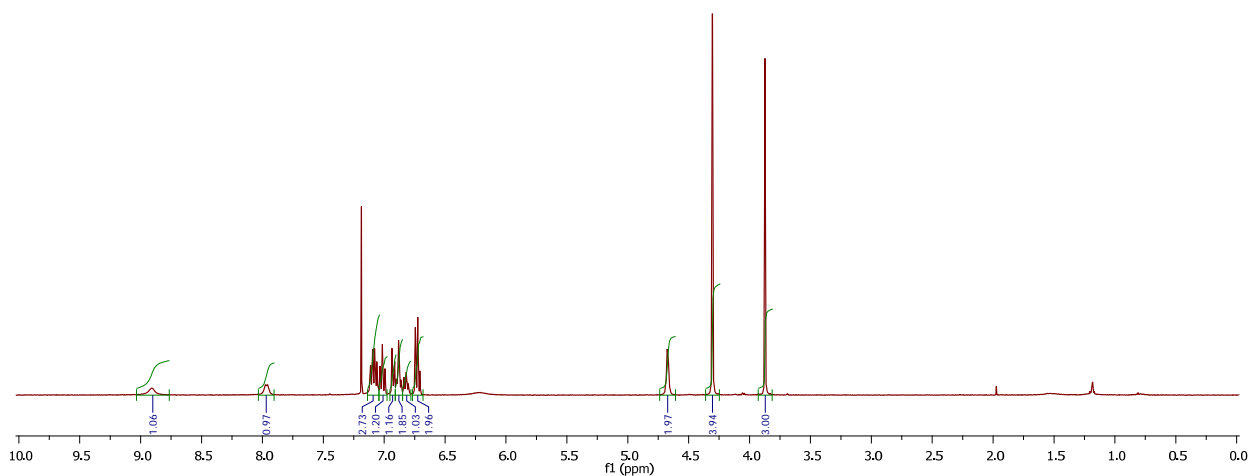
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-8-methoxy-N-(pyridin-2-ylmethyl)quinazolin-4-amine (S182). Yield: 7.4 mg, 56%. ^1H NMR (400 MHz, CDCl_3) δ 8.53 (s, 1H), 8.10 (s, 1H), 7.59 (td, J = 1.7, 7.7 Hz, 1H), 7.32 (s, br. 1H), 7.22 (d, J = 7.8 Hz, 1H), 7.18 – 7.12 (m, 1H), 7.09 (t, J = 8.0 Hz, 1H), 6.96 (d, J = 7.1 Hz, 1H), 6.93 – 6.77 (m, 3H), 4.79 (d, J = 4.6 Hz, 2H), 4.39 – 4.32 (m, 2H), 4.28 – 4.22 (m, 2H), 3.92 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.7, 156.6, 149.0, 146.3, 136.7, 124.2, 123.3, 122.4, 122.2, 119.4, 116.8, 112.2, 122.0, 111.5, 66.2, 56.1, 45.9, 42.3. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{22}\text{N}_5\text{O}_2$ ($\text{M}+\text{H}$) 400.1773; found 400.1768.

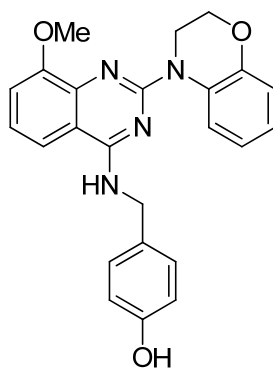




KSC-16-222

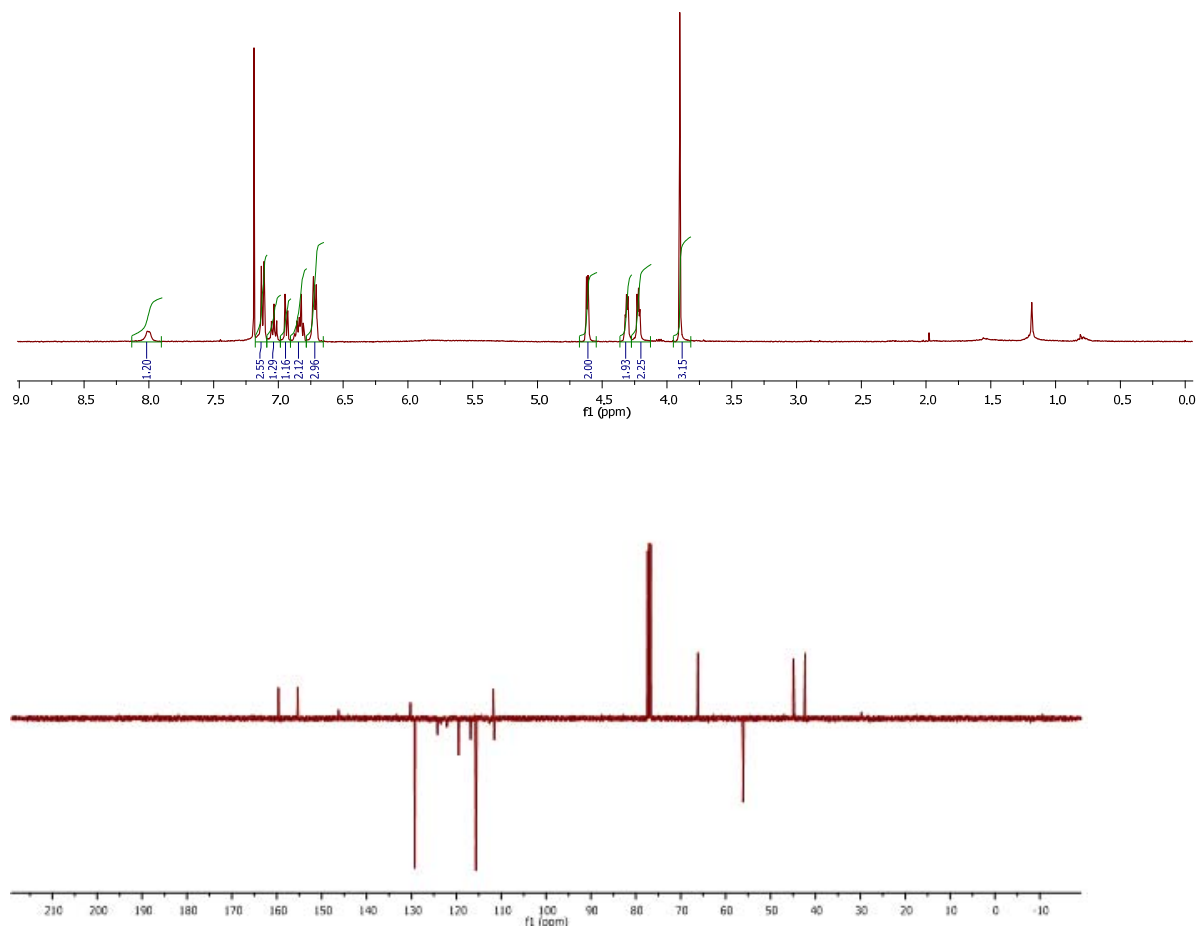
2-(((2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-8-methoxyquinazolin-4-yl)amino)methyl)phenol (S183 or 43). Yield: 11.0 mg, 51%. ^1H NMR (400 MHz, CDCl_3) δ 8.91 (s, br. 1H), 7.97 (s, br. 1H), 7.14 – 7.04 (m, 3H), 7.01 (t, $J = 7.9$ Hz, 1H), 6.93 (d, $J = 8.8$ Hz, 1H), 6.91 – 6.85 (m, 2H), 6.82 (t, $J = 7.3$ Hz, 1H), 6.73 (t, $J = 7.2$ Hz, 2H), 4.68 (s, br. 2H), 4.30 (s, 4H), 3.87 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.9, 155.8, 146.3, 130.8, 129.9, 124.0, 122.8, 119.9, 119.7, 117.4, 117.2, 112.6, 112.1, 111.7, 66.0, 56.1, 43.1, 42.0. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) 415.1770; found 415.1763.

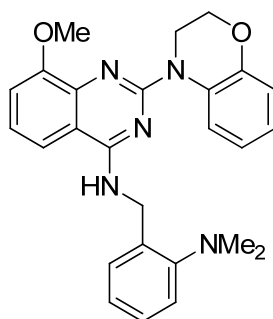




KSC-16-235

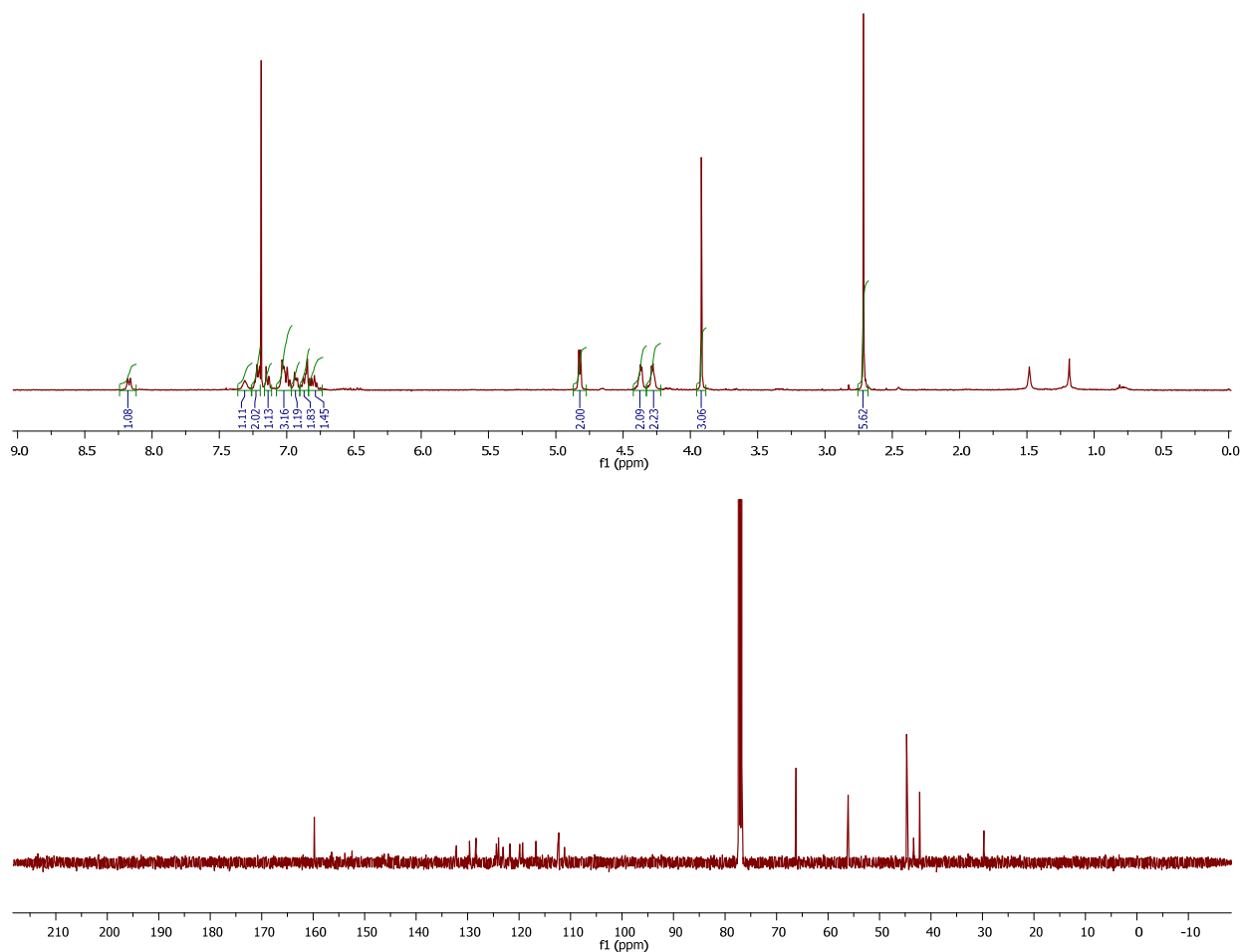
4-(((2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-8-methoxyquinazolin-4-yl)amino)methyl)phenol (S184). Yield: 7.0 mg, 36%. ^1H NMR (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.13 – 7.11 (m, 3H), 7.03 (t, $J = 8.0$ Hz, 1H), 6.94 (d, $J = 8.6$ Hz, 1H), 6.91 – 6.78 (m, 2H), 6.72 (d, $J = 8.4$ Hz, 3H), 4.62 (d, $J = 5.0$ Hz, 2H), 4.31 (d, $J = 4.5$ Hz, 2H), 4.23 (d, $J = 4.6$ Hz, 2H), 3.90 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.6, 155.3, 146.3, 130.2, 129.3, 124.2, 123.5, 122.1, 119.5, 116.8, 115.6, 112.7, 111.8, 111.6, 66.2, 56.1, 44.9, 42.3. HRMS (m/z): calcd for $\text{C}_{24}\text{H}_{23}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) 415.1770; found 415.1760.

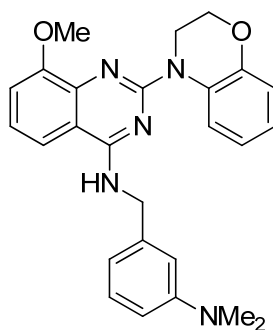




KSC-16-227

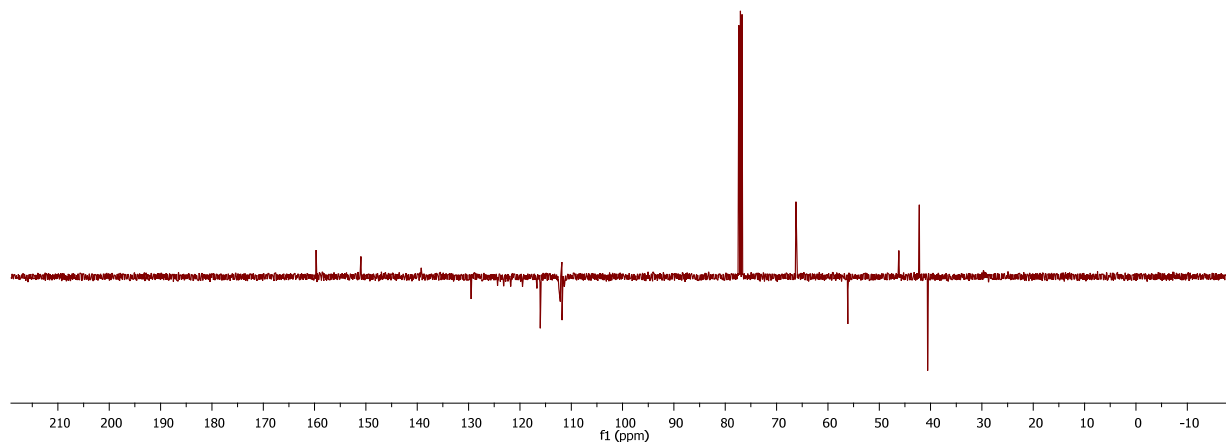
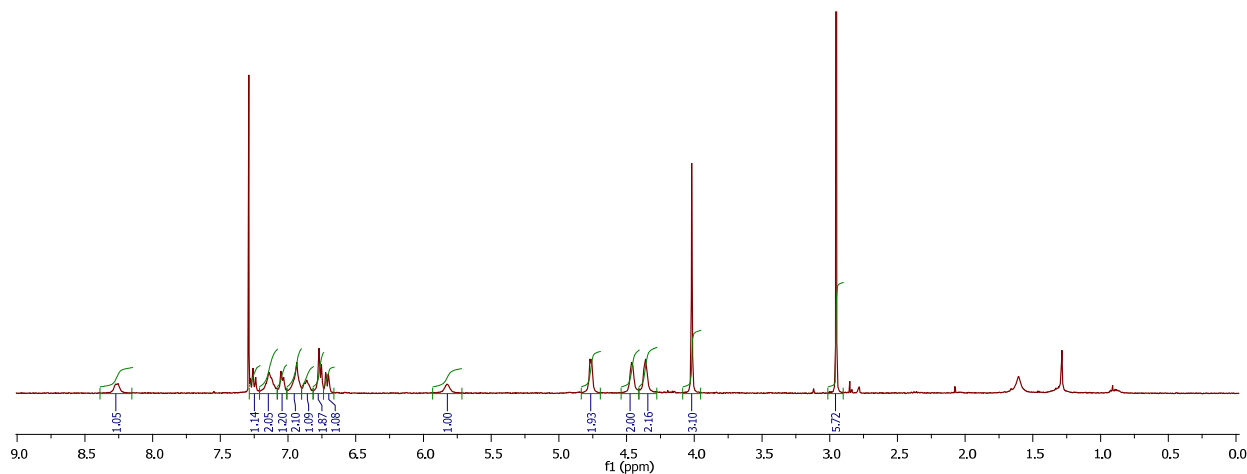
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-(2-(dimethylamino)benzyl)-8-methoxyquinazolin-4-amine (S185). Yield: 4.6 mg, 36%. ^1H NMR (400 MHz, CDCl_3) δ 8.16 (s, 1H), 7.31 (s, br. 1H), 7.21 (d, $J = 7.2$ Hz, 2H), 7.14 (d, $J = 7.5$ Hz, 1H), 7.04 – 6.97 (m, 3H), 6.94 – 6.91 (m, 1H), 6.89 – 6.85 (m, 2H), 6.84 – 6.74 (m, 1H), 4.82 (d, $J = 5.1$ Hz, 2H), 4.40 – 4.36 (m, 2H), 4.29 – 4.27 (m, 2H), 3.92 (s, 3H), 2.71 (s, 6H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.8, 132.2, 129.6, 128.4, 124.4, 124.0, 121.8, 120.0, 119.3, 116.7, 112.4, 112.3, 111.2, 66.2, 56.1, 44.7, 43.4, 42.2. HRMS (m/z): calcd for $\text{C}_{26}\text{H}_{28}\text{N}_5\text{O}_2$ (M+H) 442.2243; found 442.2233.

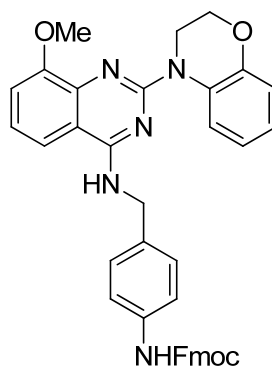




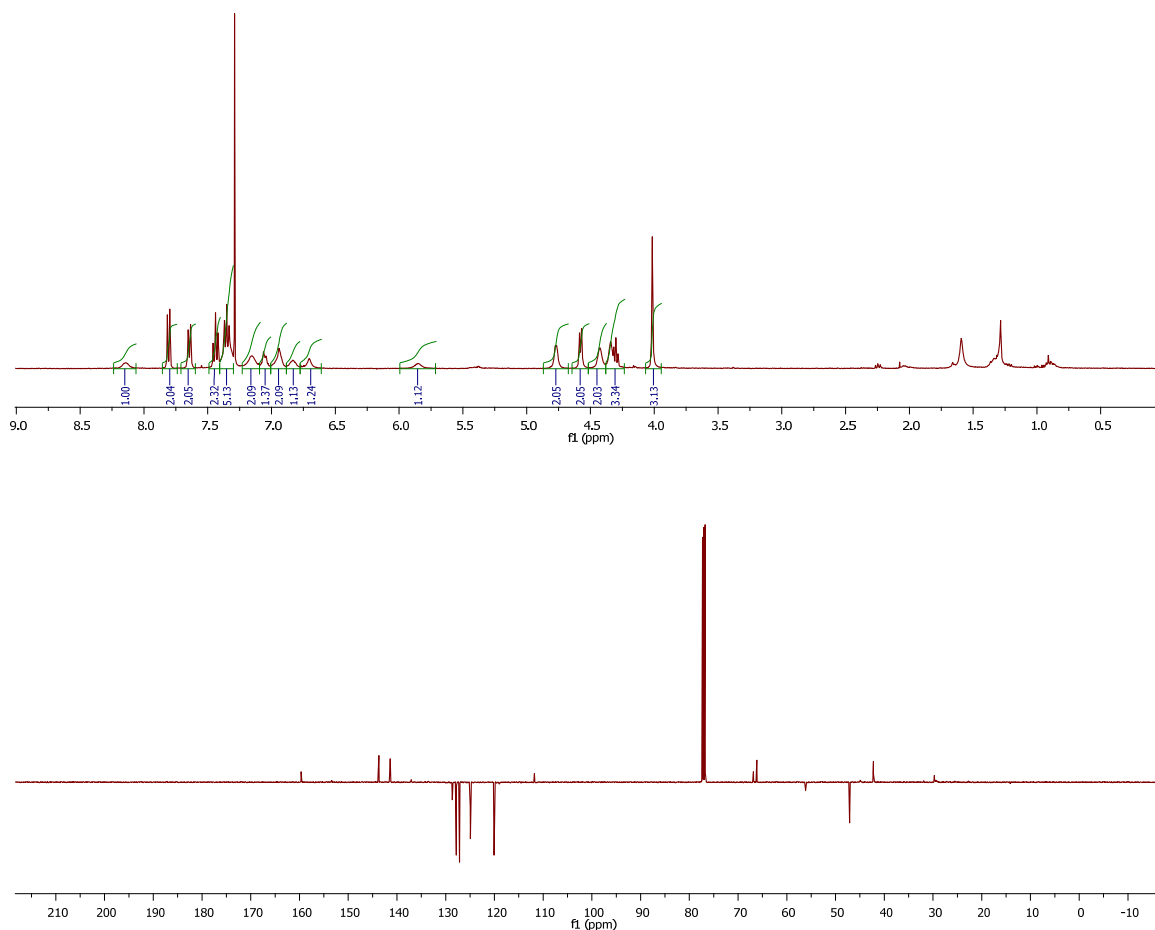
KSC-16-243

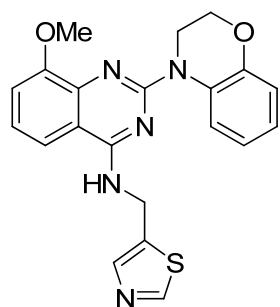
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-(3-(dimethylamino)benzyl)-8-methoxyquinazolin-4-amine (S186). Yield: 5.7 mg, 44%. ^1H NMR (400 MHz, CDCl_3) δ 8.39 – 8.15 (m, 1H), 7.26 (s, 1H), 7.14 (s, 2H), 7.05 (s, 1H), 6.94 (s, 2H), 6.90 – 6.82 (m, 1H), 6.76 (d, $J = 7.1$ Hz, 2H), 6.71 (d, $J = 8.0$ Hz, 1H), 5.93 – 5.72 (m, 1H), 4.77 (s, br. 2H), 4.46 (s, br. 2H), 4.36 (s, br. 2H), 4.02 (s, 3H), 2.95 (s, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.7, 151.0, 139.2, 129.5, 124.4, 123.1, 121.8, 119.5, 116.7, 116.0, 112.4, 112.2, 111.4, 111.8, 111.8, 66.2, 56.1, 46.2, 42.2, 40.6. HRMS (m/z): calcd for $\text{C}_{26}\text{H}_{28}\text{N}_5\text{O}_2$ ($\text{M}+\text{H}$) 442.2243; found 442.2239.





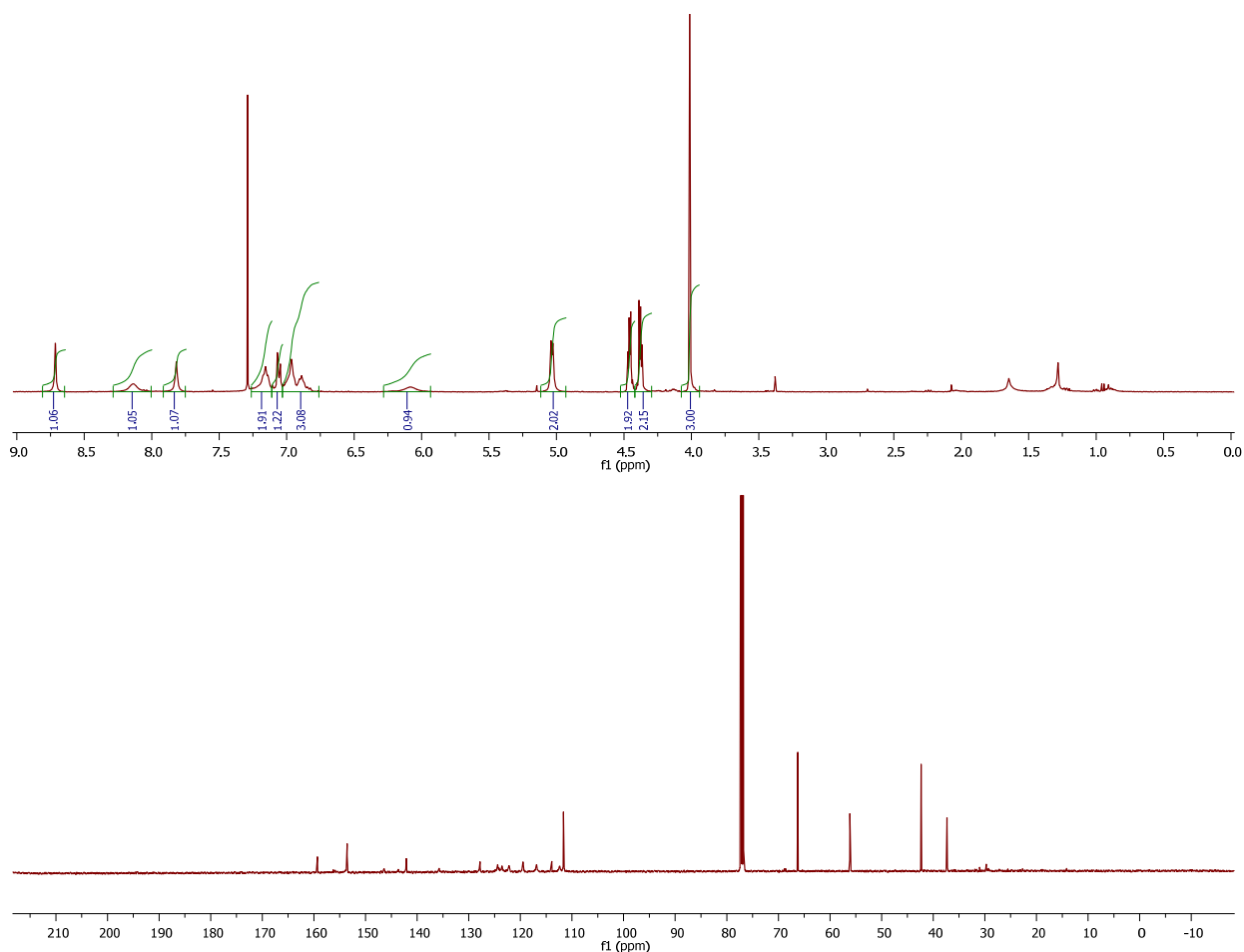
(9H-Fluoren-9-yl)methyl 4-(((2-(2H-benzo[*b*][1,4]oxazin-4(3H)-yl)-8-methoxyquinazolin-4-yl)amino)methyl)phenyl)carbamate (S187). Yield: 5.4 mg, 23%. ^1H NMR (400 MHz, CDCl_3) δ 8.24 – 8.06 (m, 1H), 7.81 (d, $J = 7.5$ Hz, 2H), 7.64 (d, $J = 7.5$ Hz, 2H), 7.44 (t, $J = 7.4$ Hz, 2H), 7.41 – 7.30 (m, 5H), 7.23 – 7.09 (m, 2H), 7.06 (s, 1H), 6.94 (s, 2H), 6.88 – 6.78 (m, 1H), 6.78 – 6.61 (m, 1H), 5.99 – 5.71 (m, 1H), 4.77 (s, br. 2H), 4.58 (d, $J = 6.5$ Hz, 2H), 4.42 (s, br. 2H), 4.34 – 4.28 (m, 3H), 4.02 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.7, 153.4, 143.7, 141.4, 137.0, 128.6, 127.8, 127.6, 127.2, 124.9, 120.1, 119.0, 111.8, 66.9, 66.2, 56.2, 47.1, 44.9, 42.2, 29.7. HRMS (m/z): calcd for $\text{C}_{39}\text{H}_{34}\text{N}_5\text{O}_4$ ($M+H$) 636.2611; found 636.2613.



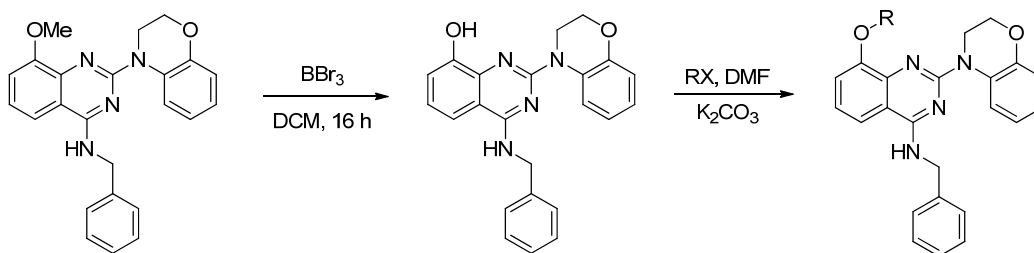


KSC-25-6

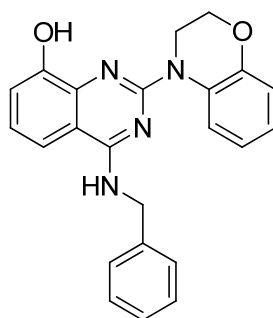
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-8-methoxy-N-(thiazol-5-ylmethyl)quinazolin-4-amine (S188). Yield: 10.1 mg, 76%. ^1H NMR (400 MHz, CDCl_3) δ 8.71 (s, 1H), 8.29 – 8.01 (m, 1H), 7.82 (s, 1H), 7.16 (s, 2H), 7.06 (d, $J = 8.6$ Hz, 1H), 6.96 – 6.84 (m, 3H), 6.28 – 5.93 (m, 1H), 5.03 (d, $J = 5.5$ Hz, 2H), 4.53 – 4.42 (m, 2H), 4.42 – 4.29 (m, 2H), 4.01 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.3, 156.0, 153.6, 146.4, 143.7, 142.1, 135.7, 127.8, 124.4, 123.6, 122.2, 119.5, 116.9, 113.9, 112.4, 111.7, 66.3, 56.1, 42.4, 37.3. HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{20}\text{N}_5\text{O}_2\text{S}$ ($\text{M}+\text{H}$) 406.1338; found 406.1341.



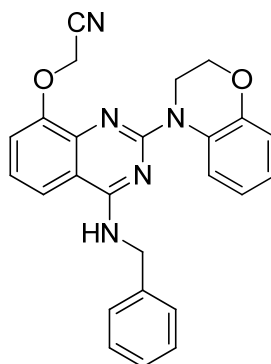
General procedure B: representative protocol for the synthesis of 8-*O*-alkylatedquinazoline analogues, synthesis and characterization for S148 (**9**), S150-S152, S154.



Scheme S2. Synthesis of 8-*O*-alkylated quinazolines

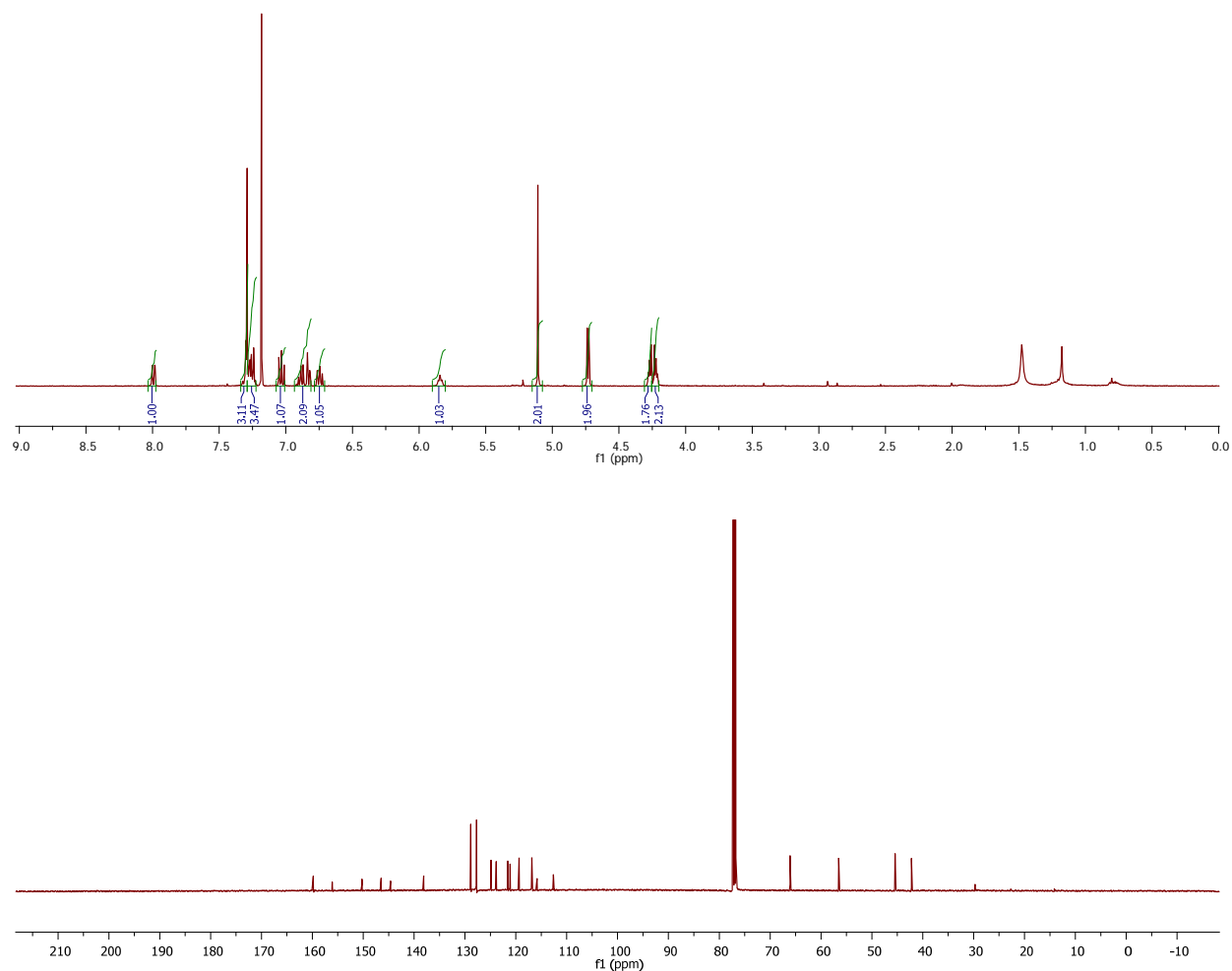


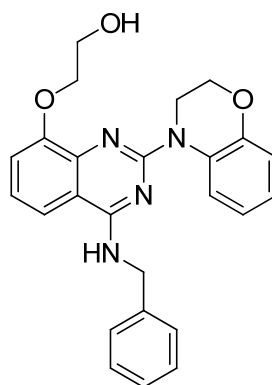
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-4-(benzylamino)quinazolin-8-ol (S148). To a solution of 2-(2H-benzo[*b*][1,4]oxazin-4(3H)-yl)-*N*-benzyl-8-methoxyquinazolin-4-amine (2.6 mg, 6.5 μ mol) in 0.5 mL of DCM at 0 °C, was added BBr₃ (39 μ L, 39 μ mol, 1M in DCM). The mixture was stirred at room temperature for 16 h. The reaction was quenched with slow addition of water. After extraction with DCM, the organic layer was dried over MgSO₄, evaporated under vacuum to give the product. Yield: 19.0 mg, 62%. ¹H NMR (400 MHz, CDCl₃) δ 7.88 (s, 1H), 7.30 (d, *J* = 4.6 Hz, 4H), 7.28 – 7.21 (m, 1H), 7.09 - 7.06 (m, 2H), 7.02 – 6.88 (m, 2H), 6.86 (d, *J* = 6.5 Hz, 1H), 6.79 – 6.74 (m, 1H), 4.76 (d, *J* = 5.4 Hz, 2H), 4.23 (s, 4H). HRMS (*m/z*): calcd for C₂₃H₂₁N₄O₂ (*M*+H) 385.1665; found 385.1657.



KSC-206-005

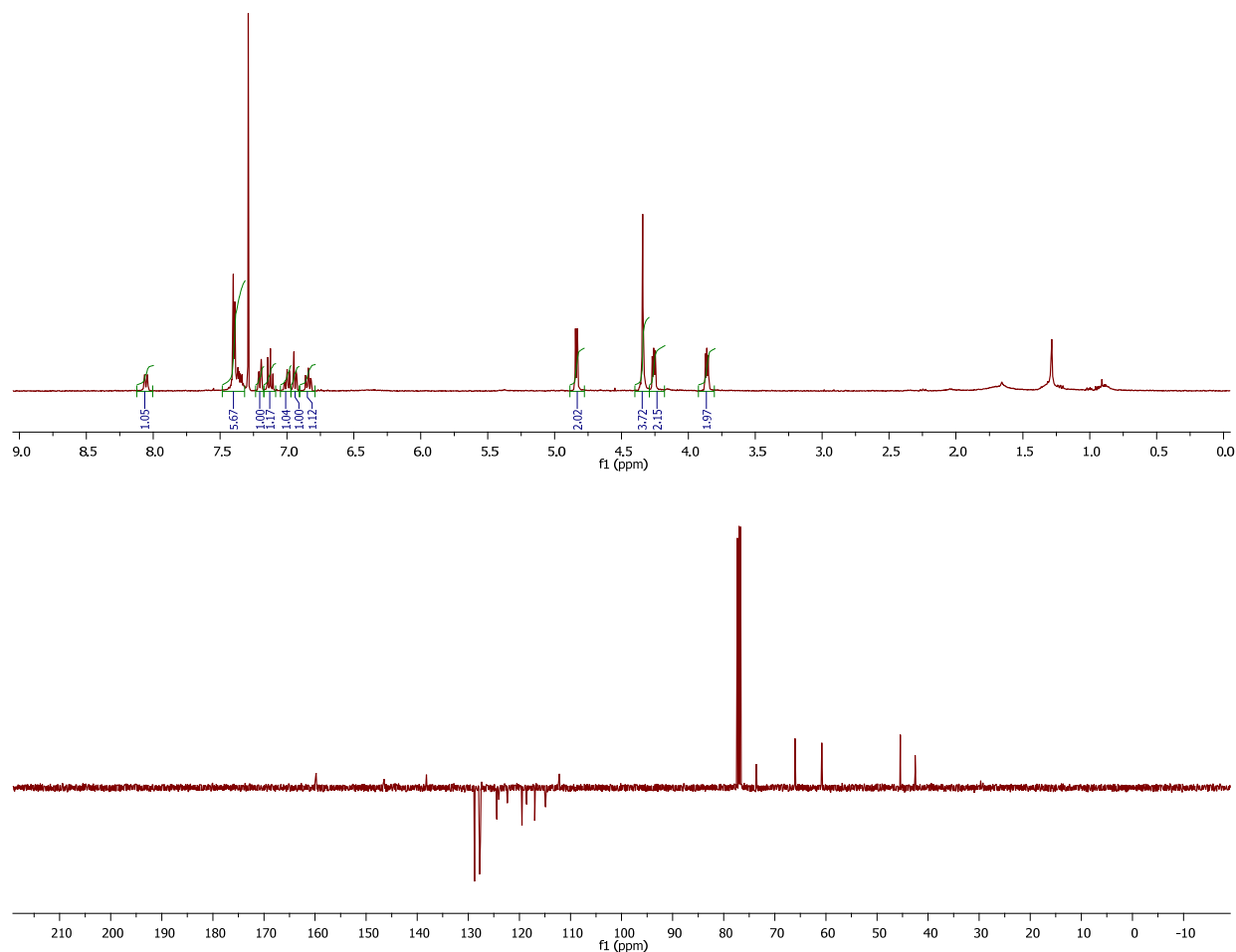
2-((2-(2*H*-Benzo[*b*][1,4]oxazin-4(3*H*)-yl)-4-(benzylamino)quinazolin-8-yl)oxy)acetonitrile (S155 or 39). To a suspension of 2-(2*H*-benzo[*b*][1,4]oxazin-4(3*H*)-yl)-4-(benzylamino)quinazolin-8-ol (0.012 g, 0.031 mmol) and K₂CO₃ (0.013 g, 0.094 mmol) in 1 mL of DMF, was added 2-chloroacetonitrile (3.0 μ L, 0.047 mmol). The mixture was stirred at 80 °C for 16 h. The reaction was monitored by LC-MS. The reaction was complete after 16 h. DMF was removed under vacuum. The product was purified by SGC (EtOAc/hexanes = 1:2, R_f = 0.6). Yield: 3.3 mg, 25%. ¹H NMR (400 MHz, CDCl₃) δ 7.99 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.34 – 7.29 (m, 3H), 7.29 – 7.22 (m, 4H), 7.07 – 7.01 (m, 1H), 6.93 – 6.81 (m, 2H), 6.79 – 6.71 (m, 1H), 5.84 (s, 1H), 5.11 (s, 2H), 4.73 (d, *J* = 5.4 Hz, 2H), 4.31 – 4.25 (m, 2H), 4.22 (dd, *J* = 3.1, 5.0 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 159.8, 156.1, 150.2, 146.5, 144.6, 138.1, 128.9, 127.7, 124.9, 123.9, 121.6, 121.1, 119.4, 116.9, 116.8, 115.8, 112.6, 66.1, 56.5, 45.5, 42.2. HRMS (*m/z*): calcd for C₂₅H₂₂N₅O₂ (M+H) 424.1773; found 424.1783.

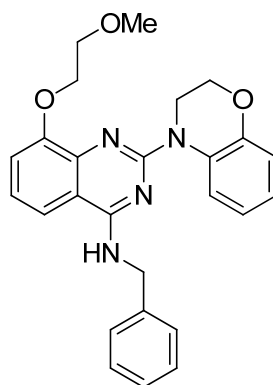




KSC-16-260

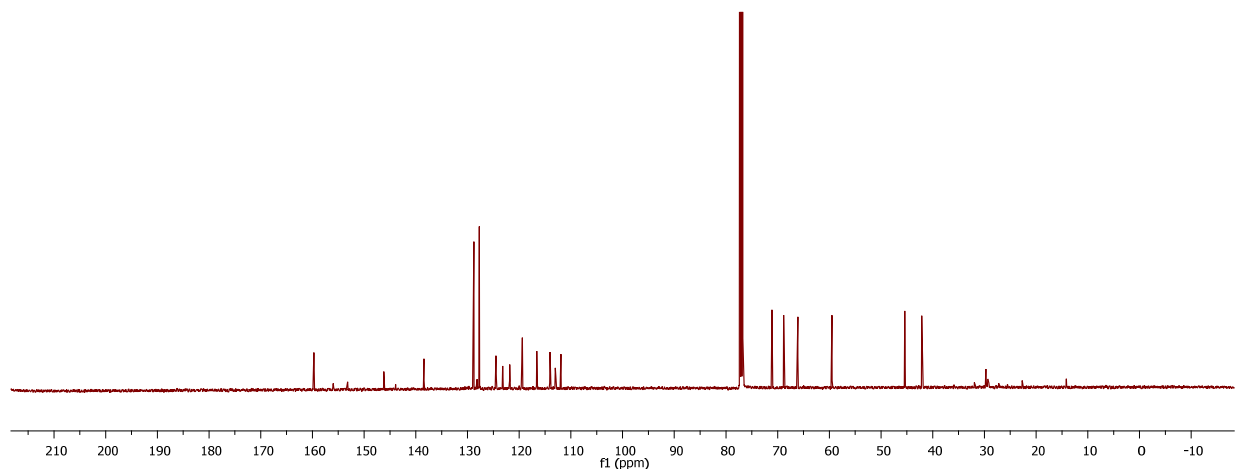
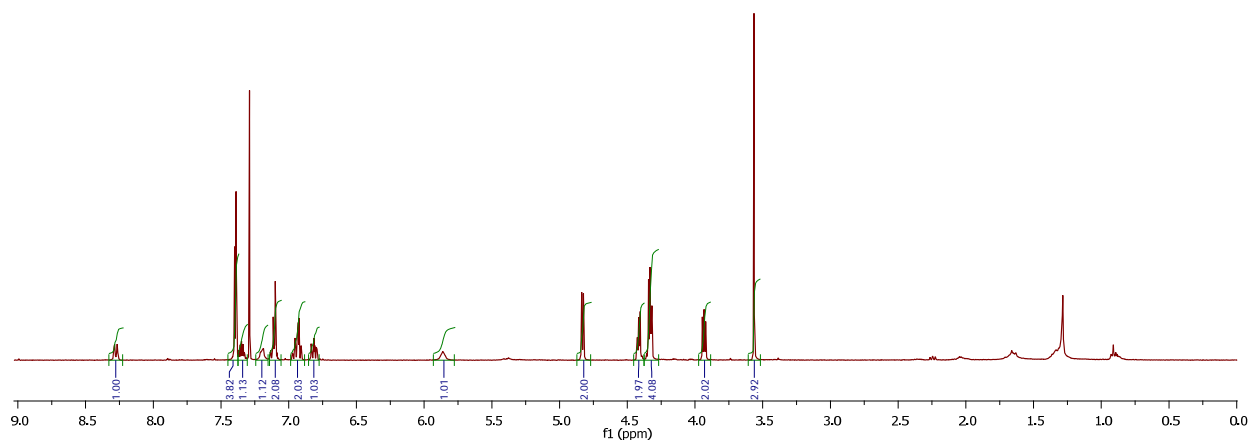
2-((2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-4-(benzylamino)quinazolin-8-yl)oxy)ethanol (S150 or 33). Yield: 3.7 mg, 33%. ^1H NMR (400 MHz, CDCl_3) δ 8.05 (d, $J = 7.3$ Hz, 1H), 7.39 (dd, $J = 5.9, 7.5$ Hz, 6H), 7.20 (d, $J = 6.7$ Hz, 1H), 7.12 (t, $J = 7.9$ Hz, 1H), 6.99 (d, $J = 6.9$ Hz, 1H), 6.97 – 6.91 (m, 1H), 6.84 (t, $J = 7.6$ Hz, 1H), 4.84 (d, $J = 5.5$ Hz, 2H), 4.34 (s, 4H), 4.29 – 4.18 (m, 2H), 3.92 – 3.81 (m, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.8, 146.5, 138.2, 128.8, 127.8, 127.6, 127.4, 124.4, 124.1, 122.4, 119.5, 118.6, 117.0, 114.9, 112.2, 73.6, 66.1, 60.8, 45.4, 42.5. HRMS (m/z): calcd for $\text{C}_{25}\text{H}_{25}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) 429.1927; found 429.1925.

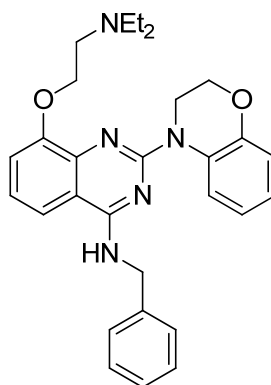




KSC-25-29

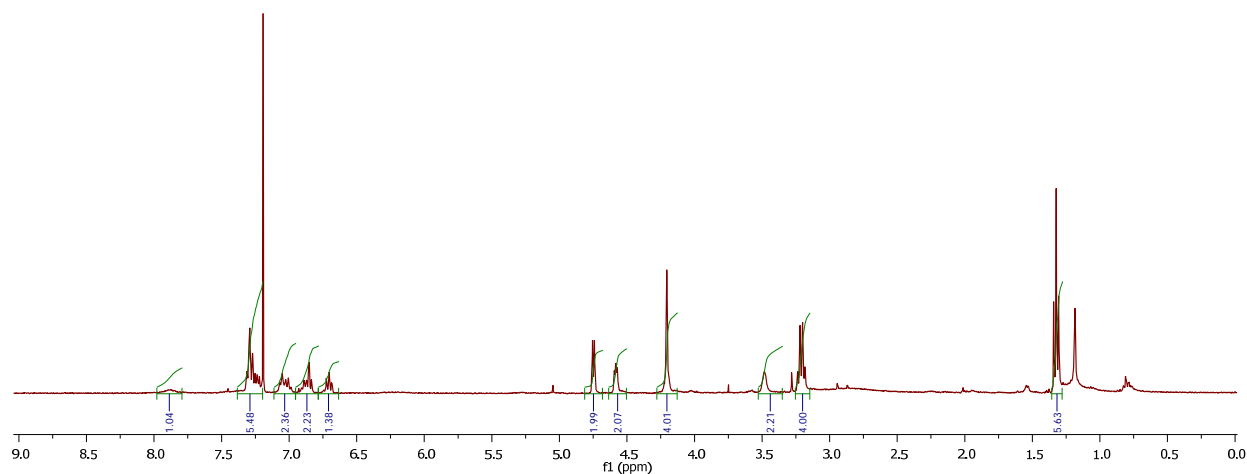
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-(2-methoxyethoxy)quinazolin-4-amine (S151 or 34). Yield: 3.6 mg, 27%. ^1H NMR (400 MHz, CDCl_3) δ 8.28 (d, $J = 7.7$ Hz, 1H), 7.40 - 7.39 (m, 4H), 7.37 - 7.32 (m, 1H), 7.21 - 7.19 (m, 1H), 7.13 - 7.09 (m, 2H), 6.99 - 6.88 (m, 2H), 6.83 - 6.79 (m, 1H), 5.86 (s, br. 1H), 4.83 (d, $J = 5.4$ Hz, 2H), 4.45 - 4.38 (m, 2H), 4.38 - 4.27 (m, 4H), 3.97 - 3.88 (m, 2H), 3.56 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.7, 156.0, 153.2, 146.2, 143.9, 138.4, 128.8, 128.1, 127.7, 127.6, 124.5, 123.2, 121.9, 119.4, 116.6, 114.0, 113.0, 111.9, 71.1, 68.8, 66.1, 59.5, 45.4, 42.1, 29.7. HRMS (m/z): calcd for $\text{C}_{26}\text{H}_{27}\text{N}_4\text{O}_3$ ($\text{M}+\text{H}$) 443.2083; found 443.2088.

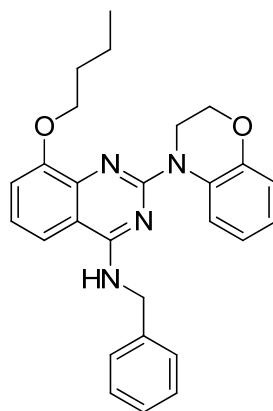




KSC-16-265

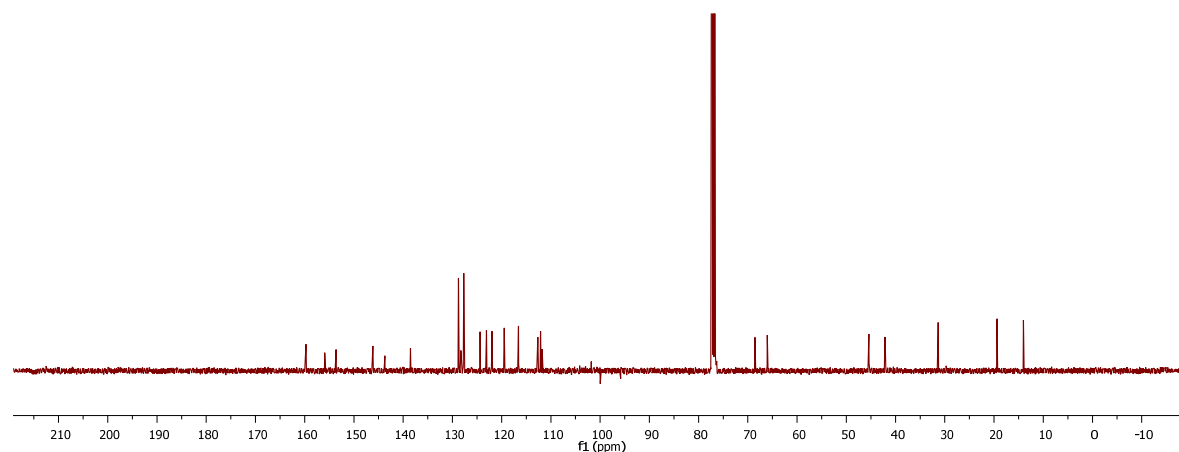
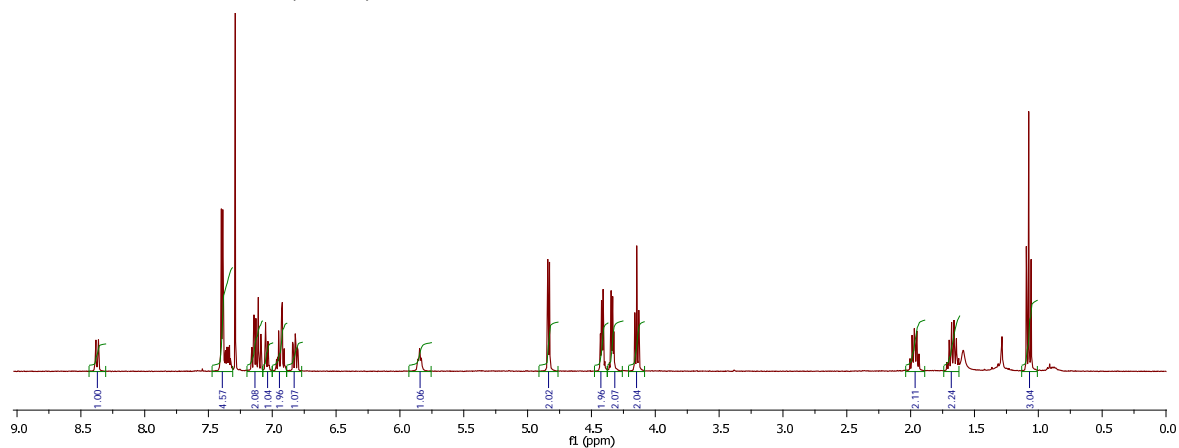
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-(2-(diethylamino)ethoxy)quinazolin-4-amine (S152 or 35). Yield: 4.1 mg, 64%. ^1H NMR (400 MHz, CDCl_3) δ 7.98 – 7.79 (m, 1H), 7.31 – 7.22 (m, 6H), 7.05 (s, 2H), 6.85 (s, 2H), 6.70 (s, 1H), 4.75 (d, $J = 5.5$, 2H), 4.58 (s, 2H), 4.21 (s, 4H), 3.48 (s, 2H), 3.21 (d, $J = 7.3$, 4H), 1.32 (t, $J = 7.3$, 6H). HRMS (m/z): calcd for $\text{C}_{29}\text{H}_{34}\text{N}_5\text{O}_2$ ($M+H$) 484.2713; found 484.2712.



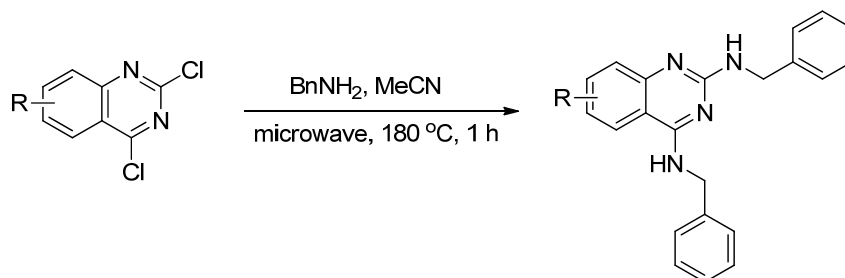


KSC-25-30

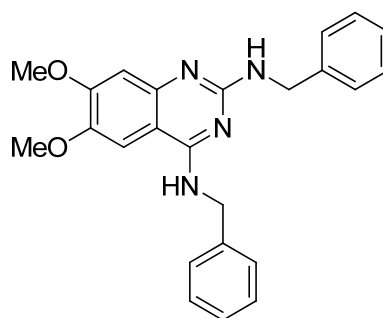
2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-butoxyquinazolin-4-amine (S154 or 37).
Yield: 4.9 mg, 61%. ^1H NMR (400 MHz, CDCl_3) δ 8.37 (d, $J = 8.2$ Hz, 1H), 7.47 – 7.31 (m, 5H), 7.20 – 7.07 (m, 2H), 7.04 (dd, $J = 1.5, 7.5$ Hz, 1H), 7.00 – 6.89 (m, 2H), 6.89 – 6.77 (m, 1H), 5.85 (s, 1H), 4.84 (d, $J = 5.4$ Hz, 2H), 4.48 – 4.38 (m, 2H), 4.35 – 4.32 (m, 2H), 4.15 (t, $J = 6.5$ Hz, 2H), 2.04 – 1.89 (m, 2H), 1.72 – 1.62 (m, 2H), 1.08 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.7, 155.9, 153.6, 146.2, 143.7, 138.5, 128.8, 128.3, 127.7, 127.6, 124.4, 123.1, 121.9, 119.5, 116.6, 112.7, 112.1, 111.8, 68.6, 66.1, 45.4, 42.1, 31.4, 19.4, 14.0. HRMS (m/z): calcd for $\text{C}_{27}\text{H}_{29}\text{N}_4\text{O}_2$ ($\text{M}+\text{H}$) 441.2291; found 441.2296.



General Procedure C: representative protocol for the one-pot synthesis of quinazoline analogues, synthesis and characterization for S129, S126-S128, S130-S141.

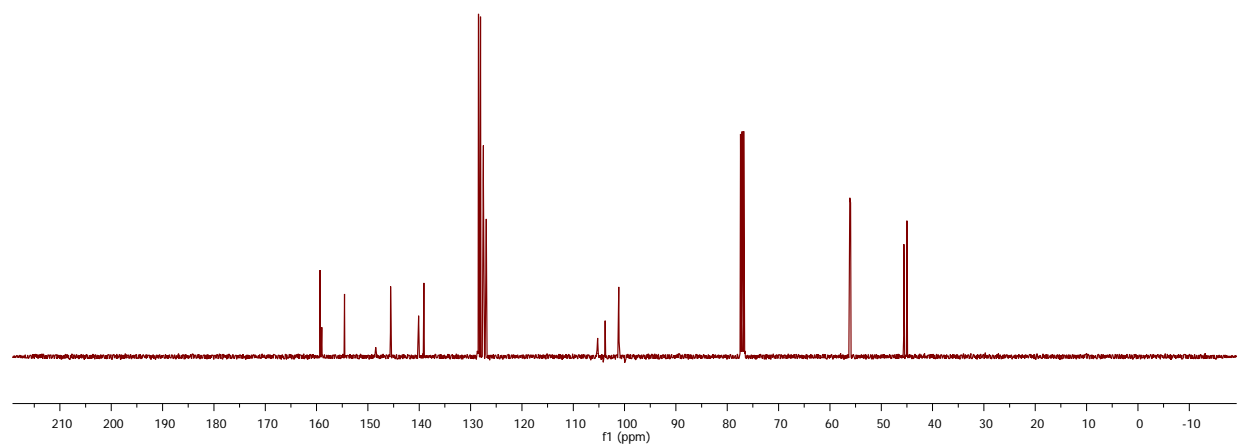
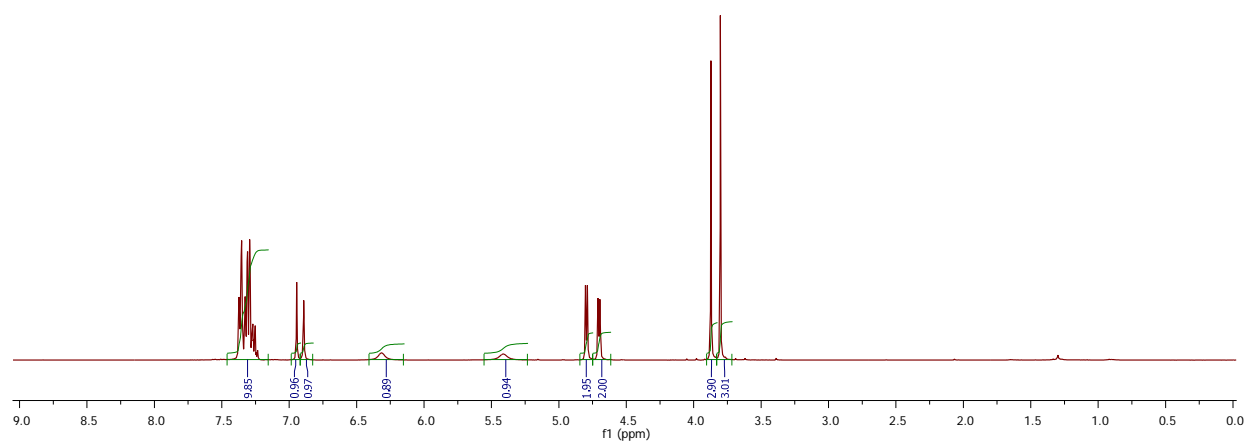


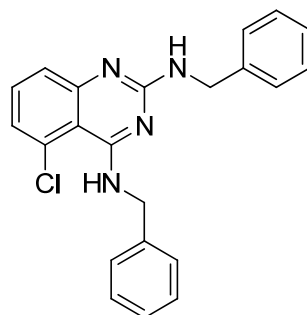
Scheme S3. Quinazoline synthesis via the one-pot protocol.



KSC-16-102

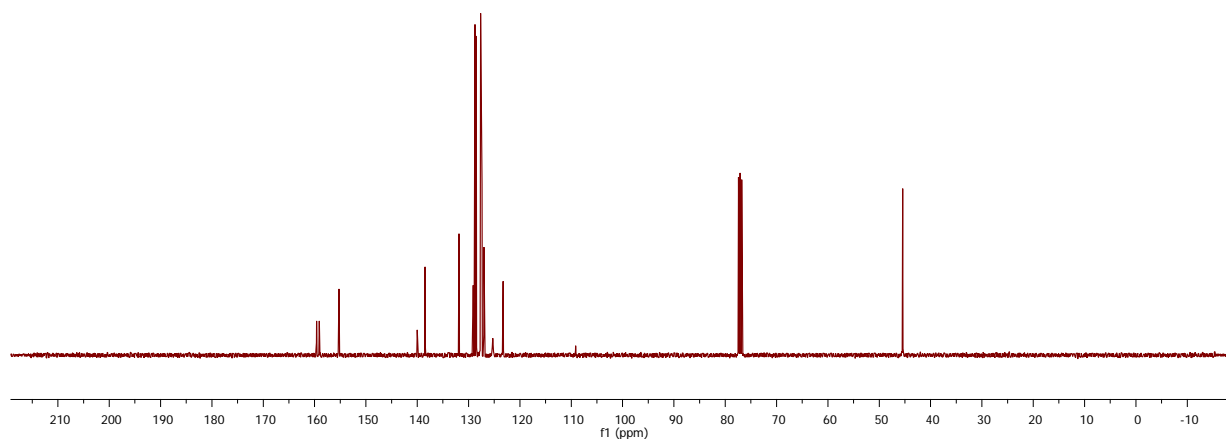
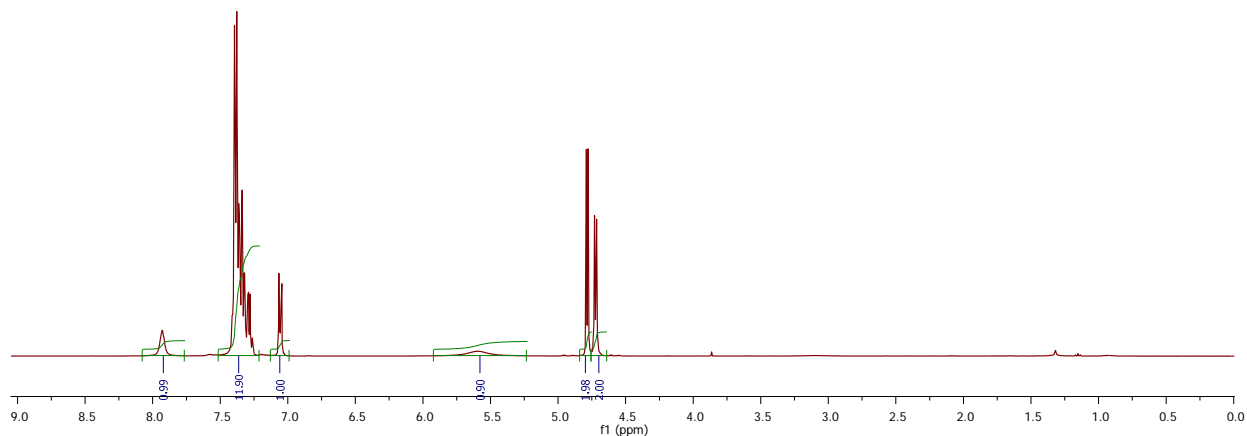
***N*²,*N*⁴-Dibenzyl-6,7-dimethoxyquinazoline-2,4-diamine (S129).** To a suspension of 2,4-dichloro-6,7-dimethoxyquinazoline (50.0 mg, 0.19 mmol) in CH₃CN (2 mL) was added benzylamine (0.11 mL, 0.96 mmol, 5 equiv.). The mixture was heated to 180 °C for 1 h under microwave irradiation. The solvent was removed under vacuum, the residue was suspended in EtOAc, washed with saturated NaHCO₃, and the layers were separated. The organic layer was dried over MgSO₄ and concentrated under vacuum. The residue was purified by SGC (EtOAc, R_f = 0.5) to give the product (66.0 mg, 85%). ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.16 (m, 10H), 6.94 (s, 1H), 6.89 (s, 1H), 6.31 (s, 1H), 5.41 (s, 1H), 4.80 (d, *J* = 5.5 Hz, 2H), 4.70 (d, *J* = 5.7 Hz, 2H), 3.87 (s, 3H), 3.80 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.3, 159.0, 154.6, 148.5, 145.6, 140.1, 139.1, 128.6, 128.5, 128.1, 127.5, 127.4, 126.9, 105.3, 103.8, 101.1, 56.1, 56.0, 45.6, 45.0. HRMS (*m/z*): calcd for C₂₄H₂₅N₄O₂ (*M*+*H*) 401.1978; found 401.1978.

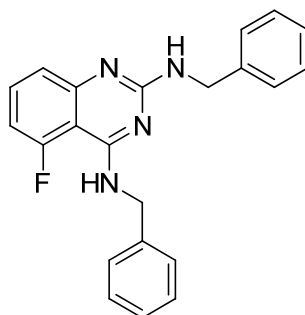




KSC-16-114

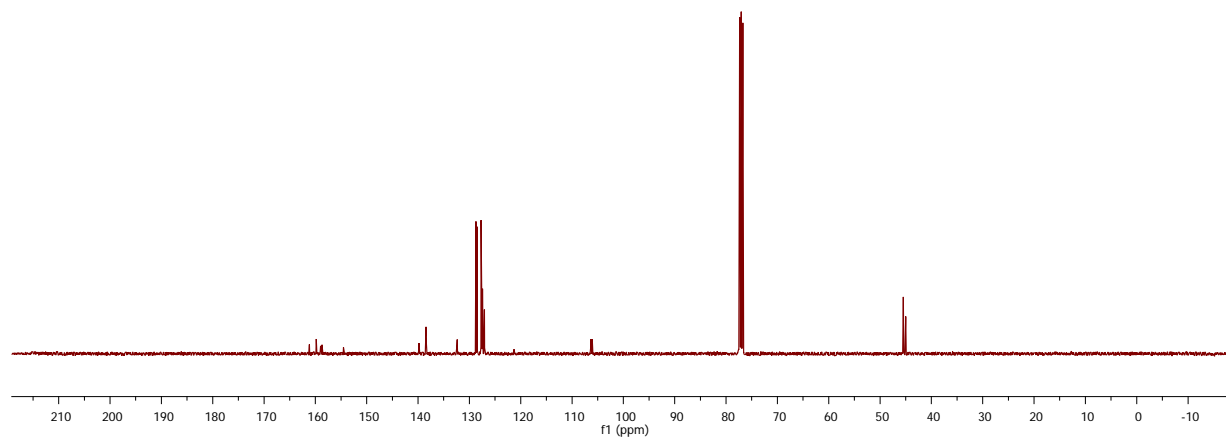
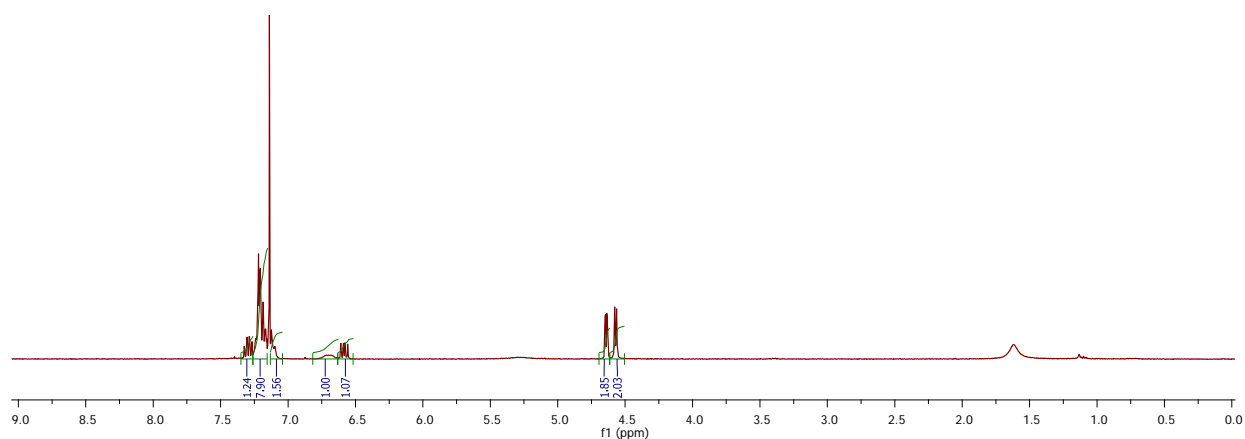
***N*²,*N*⁴-Dibenzyl-5-chloroquinazoline-2,4-diamine (S126).** Yield: 66.0 mg, 82%. ¹H NMR (400 MHz, CDCl₃) δ 7.93 (s, br. 1H), 7.51 – 7.21 (m, 12H), 7.06 (dd, *J* = 2.5, 6.3 Hz, 1H), 5.60 (s, br. 1H), 4.78 (d, *J* = 5.2 Hz, 2H), 4.72 (d, *J* = 6.0 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 159.6, 159.1, 155.2, 140.0, 138.5, 131.9, 129.1, 128.7, 128.5, 127.7, 127.6, 127.4, 127.0, 125.3, 123.3, 109.1, 45.6, 45.4. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+*H*) 375.1376; found 375.1377.

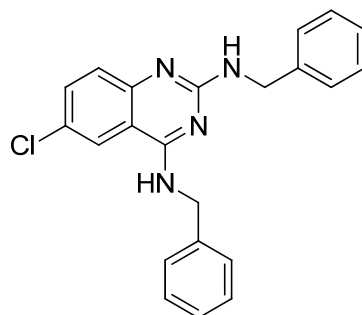




KSC-16-115

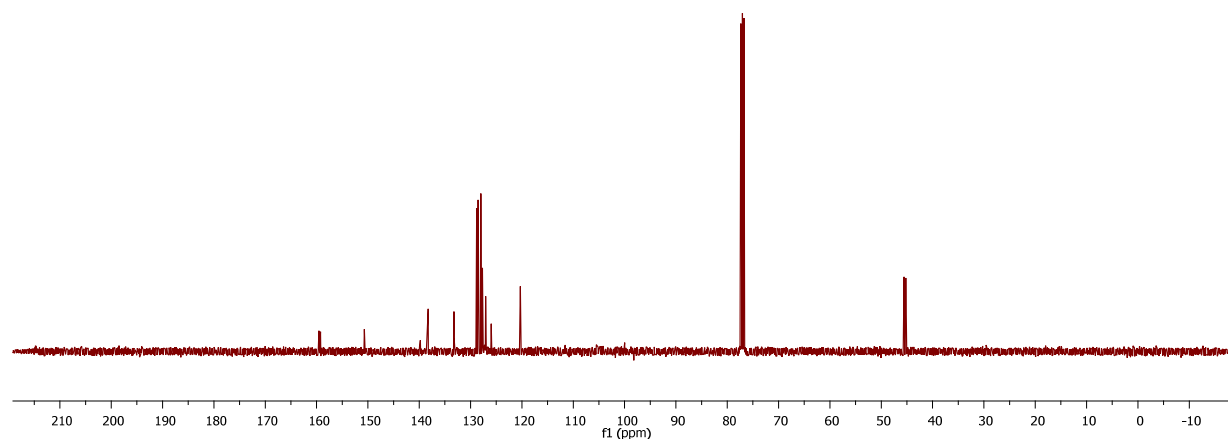
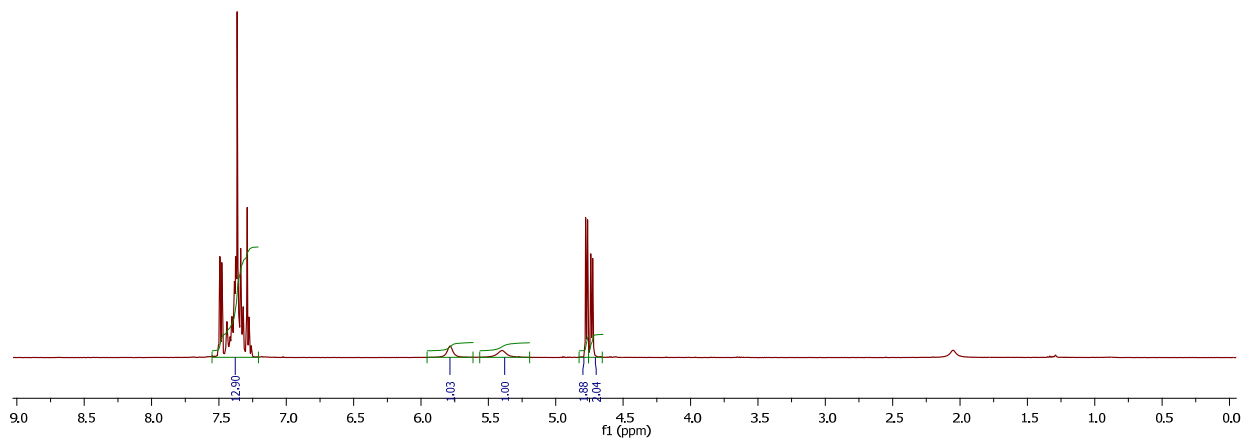
***N*²,*N*⁴-Dibenzyl-5-fluoroquinazoline-2,4-diamine (S127).** Yield: 12.8 mg, 39%. ¹H NMR (400 MHz, CDCl₃) δ 7.30 (dd, *J* = 8.2, 14.8 Hz, 1H), 7.22 – 7.17 (m, 8H), 7.12 – 7.08 (m, 2H), 6.82 – 6.63 (m, 1H), 6.58 (dd, *J* = 7.9, 12.7 Hz, 1H), 4.69 – 4.61 (m, 2H), 4.57 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 161.2, 159.8, 159.0, 158.7, 154.5, 139.8, 138.5, 132.5, 132.4, 128.7, 128.5, 127.7, 127.6, 127.5, 127.1, 121.3, 106.3, 106.1, 45.5, 45.0. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1676.

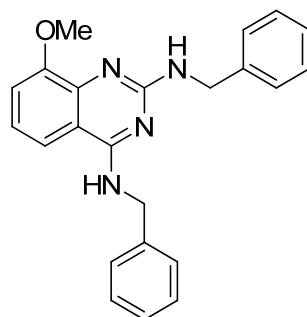




KSC-16-117

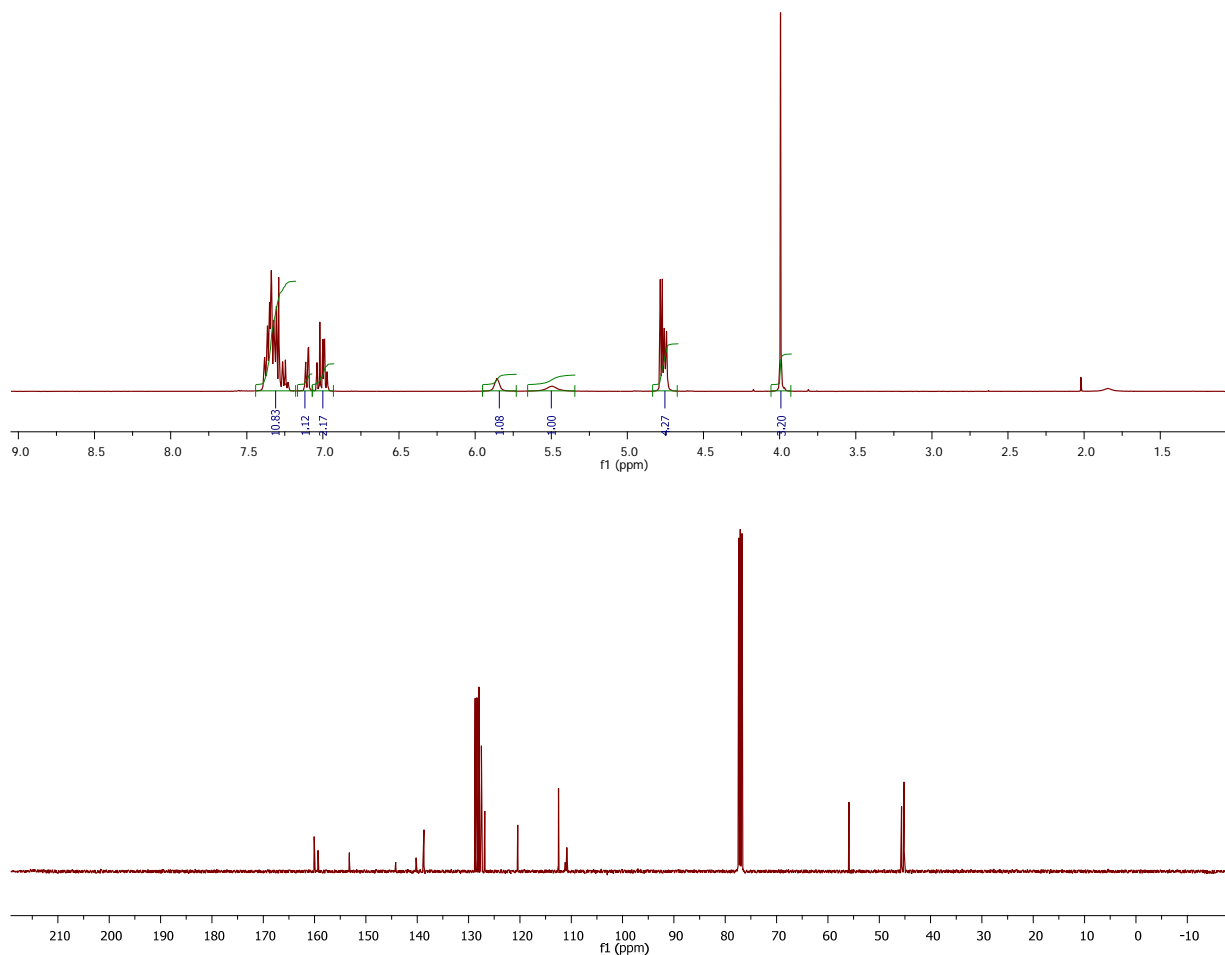
***N*²,*N*⁴-Dibenzyl-6-chloroquinazoline-2,4-diamine (S128).** Yield: 56.0 mg, 70%. ¹H NMR (400 MHz, CDCl₃) δ 7.55 – 7.21 (m, 13H), 5.78 (s, br. 1H), 5.40 (s, br. 1H), 4.77 (d, *J* = 5.4 Hz, 2H), 4.73 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 159.5, 159.2, 150.7, 139.8, 138.3, 133.2, 128.8, 128.5, 128.0, 127.7, 127.6, 127.2, 127.1, 126.0, 120.3, 45.6, 45.2. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+H) 375.1376; found 375.1376.

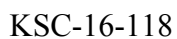


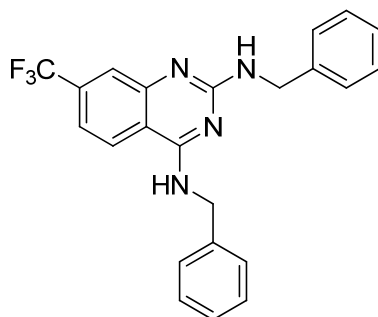


KSC-16-121

***N*²,*N*⁴-Dibenzyl-8-methoxyquinazoline-2,4-diamine (S130 or 14).** Yield: 14.9 mg, 18%. ¹H NMR (400 MHz, CDCl₃) δ 7.44 – 7.18 (m, 11H), 7.11 (dd, *J* = 1.6, 7.9 Hz, 1H), 7.07 – 6.93 (m, 2H), 5.86 (s, br. 1H), 5.49 (s, br. 1H), , 4.78 (d, *J* = 5.7 Hz, 2H), 4.75 (d, *J* = 5.7 Hz, 2H), 3.99 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.3, 153.2, 144.2, 140.2, 138.7, 128.7, 128.4, 128.0, 127.5, 126.8, 120.4, 112.5, 111.2, 110.9, 55.9, 45.7, 45.2. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (*M*+*H*) 371.1872; found 371.1871.

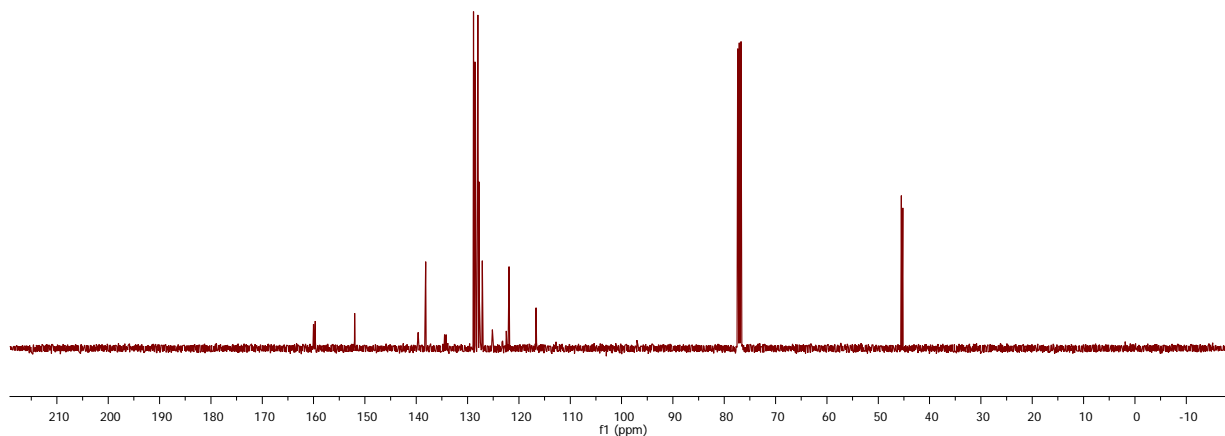
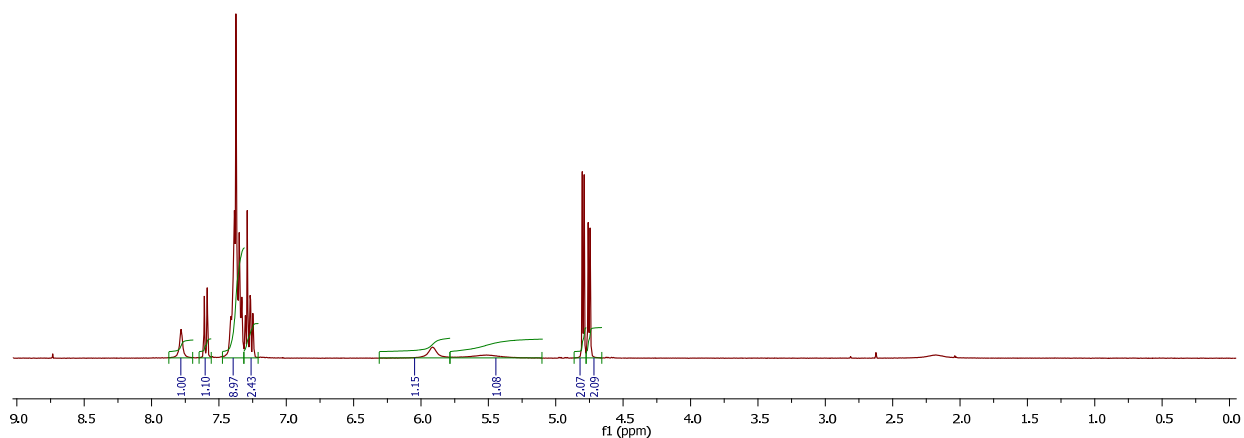


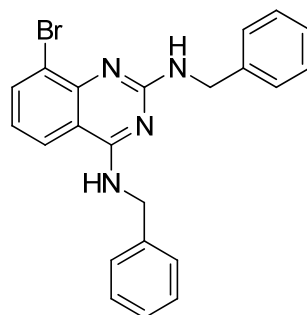




KSC-16-160c

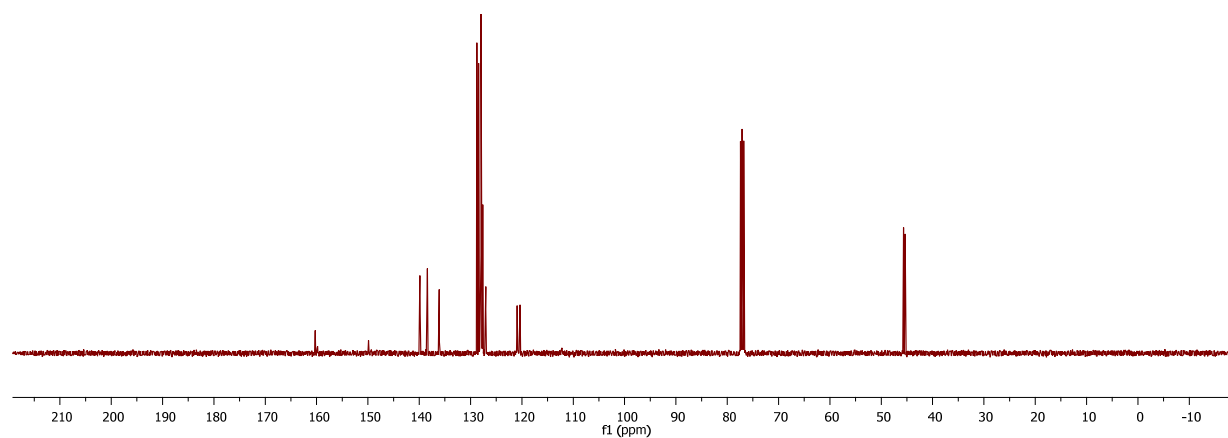
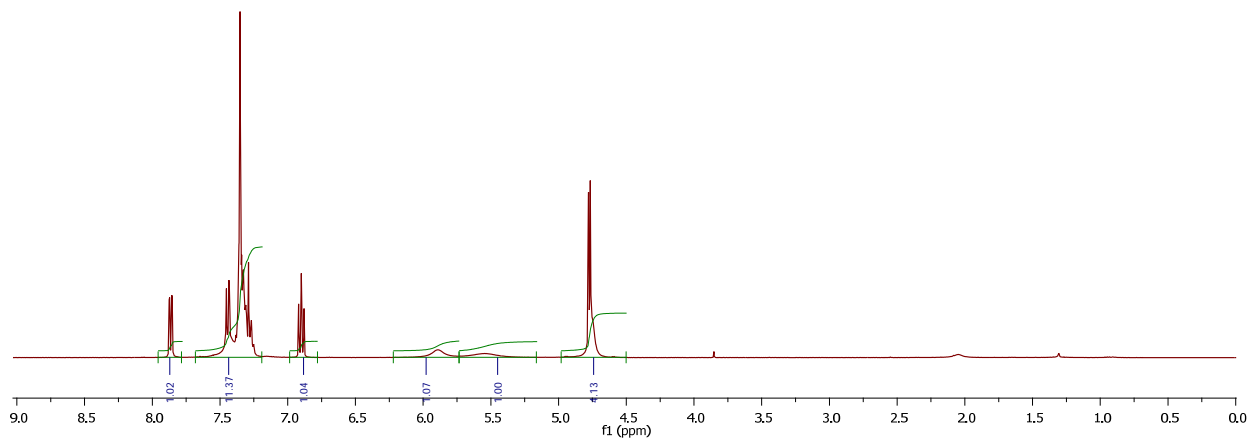
***N*²,*N*⁴-Dibenzyl-7-(trifluoromethyl)quinazoline-2,4-diamine (S132).** Yield: 75.0 mg, 98%. ¹H NMR (400 MHz, CDCl₃) δ 7.78 (s, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.39 – 7.33 (m, 9H), 7.32 – 7.21 (m, 2H), 5.91 (s, br. 1H), 5.51 (s, br. 1H), 4.80 (d, *J* = 5.4 Hz, 2H), 4.75 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 159.7, 152.0, 139.6, 138.2, 134.8, 134.5, 134.2, 133.9, 128.8, 128.6, 128.0, 127.8, 127.6, 127.1, 125.2, 123.2, 122.5, 121.9, 119.7, 116.64, 116.61, 112.8, 45.5, 45.2. HRMS (*m/z*): calcd for C₂₃H₂₀F₃N₄ (*M*+*H*) 409.1640; found 409.1642.

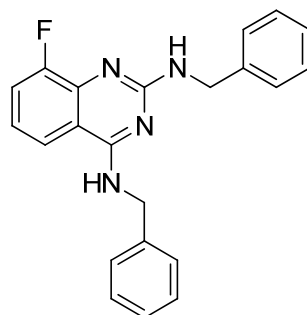




KSC-16-153

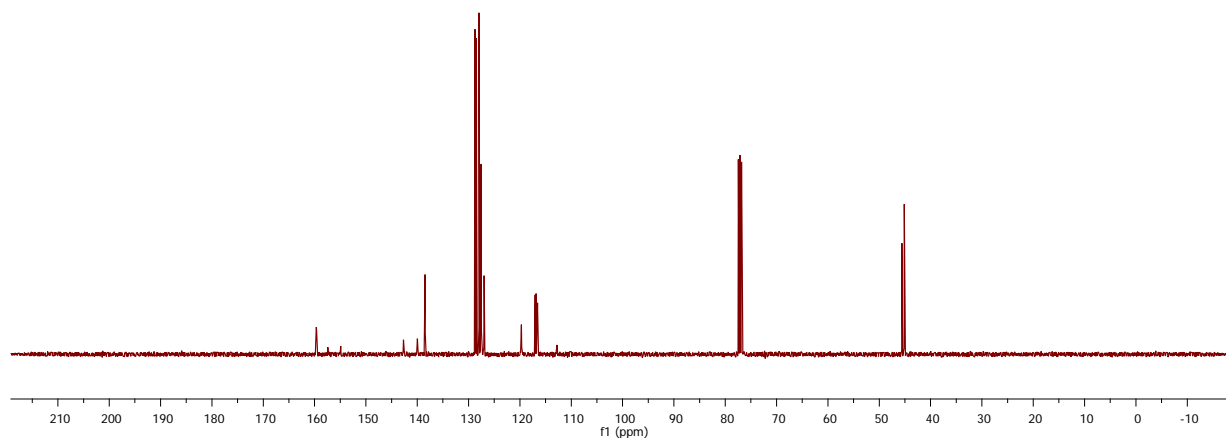
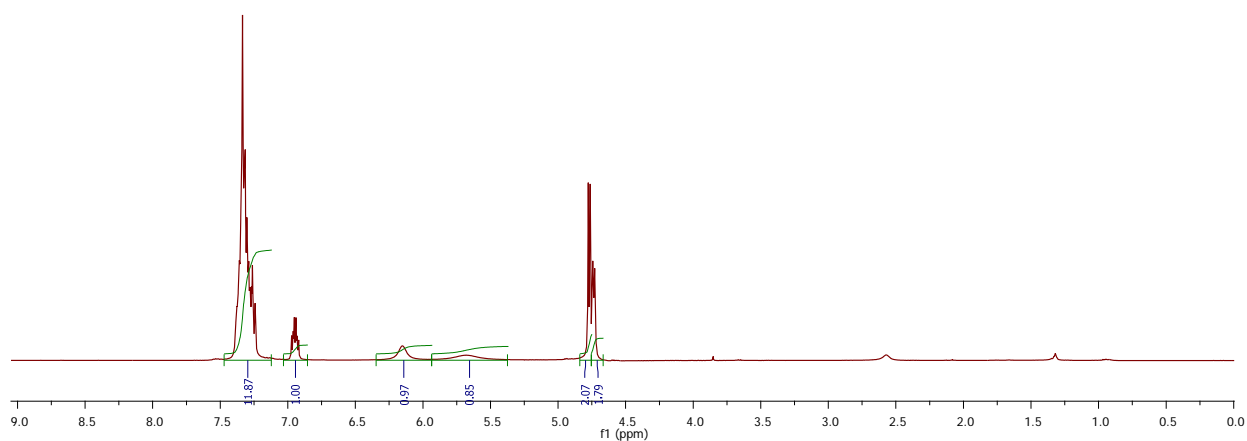
***N*²,*N*⁴-Dibenzyl-8-bromoquinazoline-2,4-diamine (S133).** Yield: 75.0 mg, 99%. ¹H NMR (400 MHz, CDCl₃) δ 7.86 (dd, *J* = 1.1, 7.6 Hz, 1H), 7.68 – 7.19 (m, 11H), 6.90 (t, *J* = 7.8 Hz, 1H), 5.89 (s, br. 1H), 5.74 – 5.16 (m, 1H), 4.77 (d, *J* = 5.4 Hz, 4H). ¹³C NMR (101 MHz, CDCl₃) δ 160.3, 159.8, 149.9, 139.9, 138.4, 136.1, 128.8, 128.4, 128.0, 127.6, 127.0, 120.9, 120.4, 45.7, 45.3. HRMS (*m/z*): calcd for C₂₂H₂₀BrN₄ (M+H) 419.0871 and 421.0851; found 421.0848.

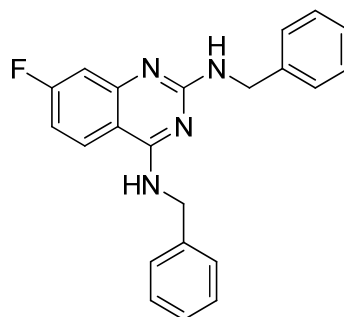




KSC-16-154

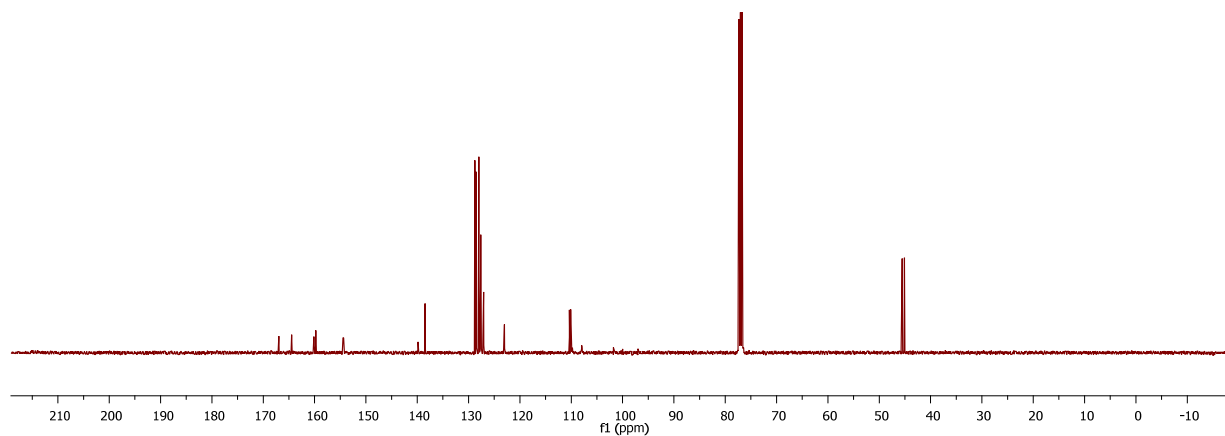
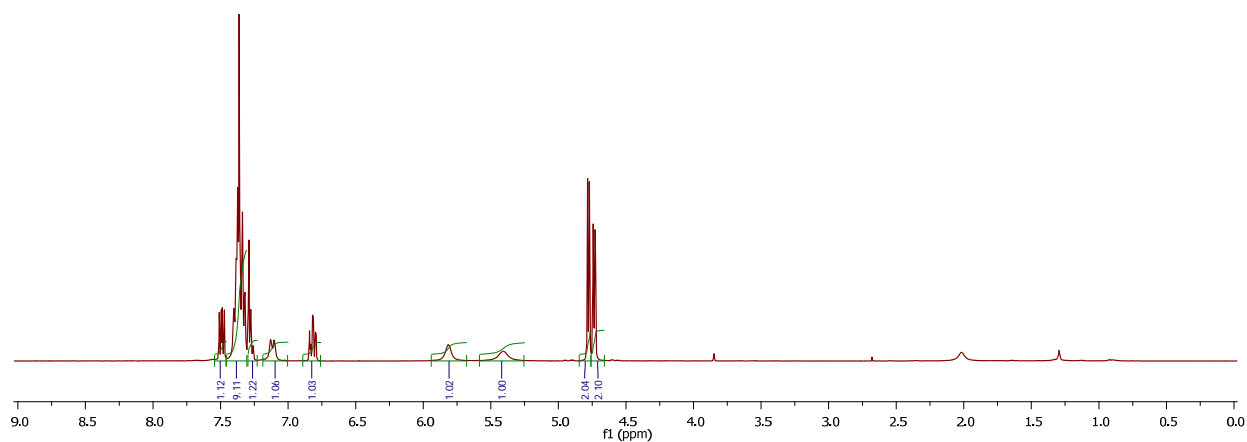
***N*²,*N*⁴-Dibenzyl-8-fluoroquinazoline-2,4-diamine (S134).** Yield: 70.0 mg, 85%. ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.12 (m, 12H), 6.95 (td, *J* = 4.9, 8.0 Hz, 1H), 6.15 (s, br. 1H), 5.68 (s, br. 1H), 4.77 (d, *J* = 5.5 Hz, 2H), 4.74 (d, *J* = 5.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 159.7, 159.6, 157.4, 154.9, 142.7, 142.6, 140.0, 138.5, 128.7, 128.5, 128.0, 127.6, 127.0, 119.8, 119.7, 117.0, 116.9, 116.6, 116.6, 112.8, 45.6, 45.1. . HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (M+H) 359.1672; found 359.1675.

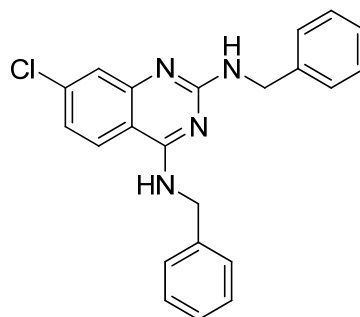




KSC-16-156

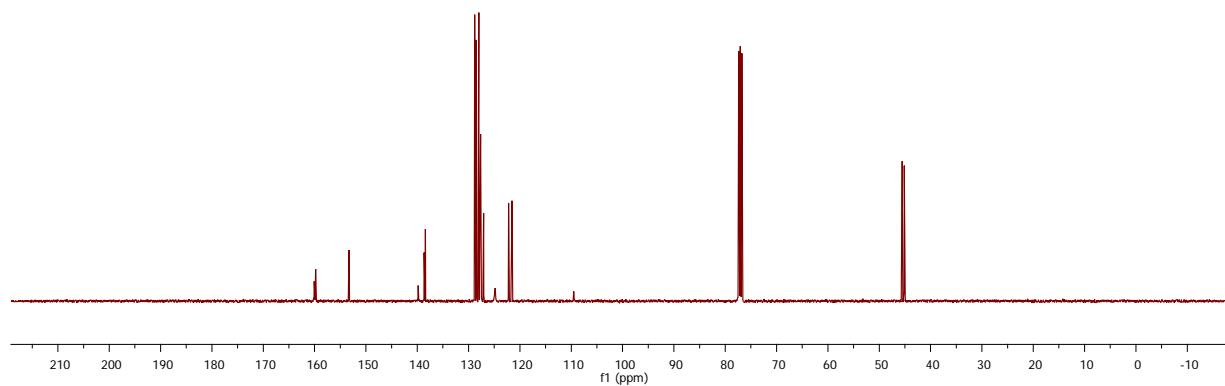
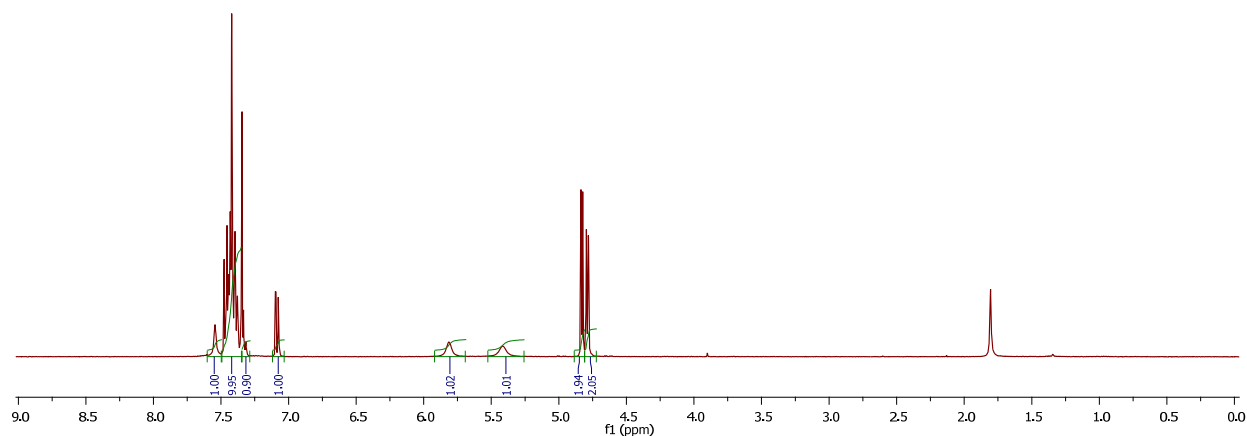
***N*²,*N*⁴-Dibenzyl-7-fluoroquinazoline-2,4-diamine (S135).** Yield: 37.0 mg, 45%. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, *J* = 5.9, 9.0 Hz, 1H), 7.46 – 7.31 (m, 9H), 7.30 – 7.23 (m, 1H), 7.12 (d, *J* = 10.3 Hz, 1H), 6.82 (td, *J* = 2.5, 8.6 Hz, 1H), 5.81 (s, br. 1H), 5.41 (s, br. 1H), 4.78 (d, *J* = 5.4 Hz, 2H), 4.73 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 167.0, 164.5, 160.1, 159.8, 154.5, 154.3, 139.8, 138.5, 128.8, 128.5, 128.0, 127.6, 127.1, 123.1, 123.0, 110.4, 110.1, 45.5, 45.1. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1674.

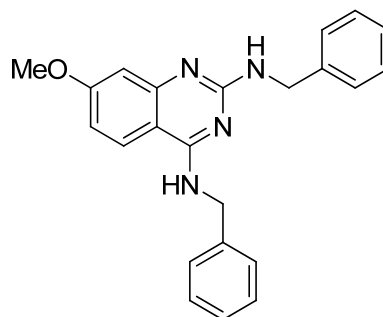




KSC-16-159

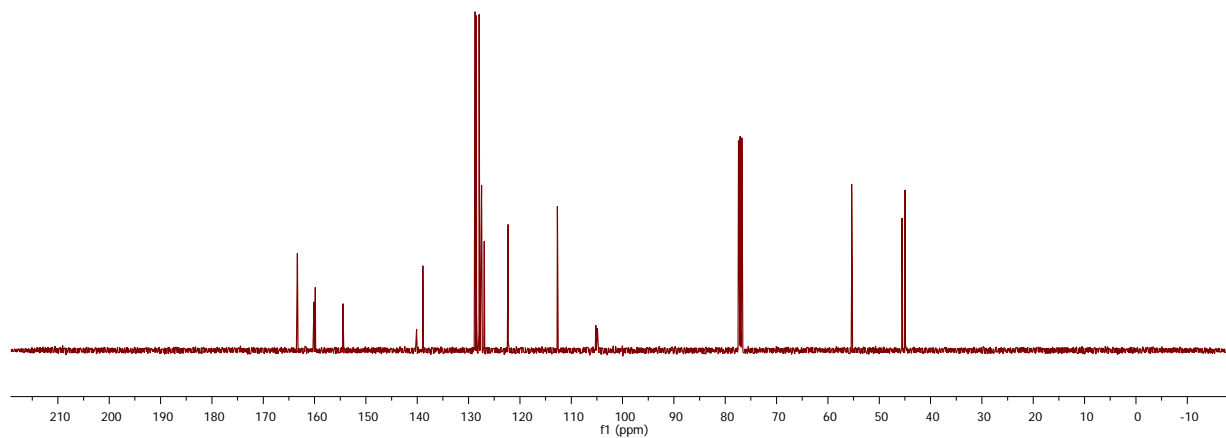
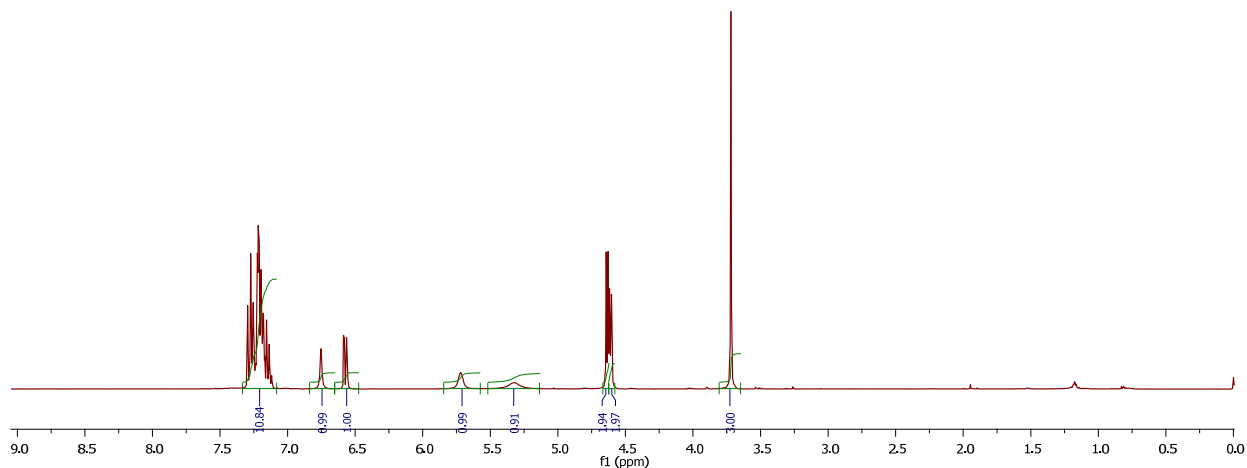
***N*²,*N*⁴-Dibenzyl-7-chloroquinazoline-2,4-diamine (S136).** Yield: 74.0 mg, 92%. ¹H NMR (400 MHz, CDCl₃) δ 7.54 (s, br. 1H), 7.50 – 7.37 (m, 10H), 7.32 (d, *J* = 7.0 Hz, 1H), 7.08 (dd, *J* = 2.1, 8.7 Hz, 1H), 5.82 (s, br. 1H), 5.42 (s, br. 1H), 4.83 (d, *J* = 5.4 Hz, 2H), 4.79 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 159.8, 153.3, 139.8, 138.7, 138.4, 128.8, 128.5, 128.0, 127.7, 127.6, 127.1, 124.8, 122.2, 121.6, 109.5, 45.5, 45.1. HRMS (*m/z*): calcd for C₂₂H₂₀ClN₄ (*M*+*H*) 375.1376; found 375.1377.

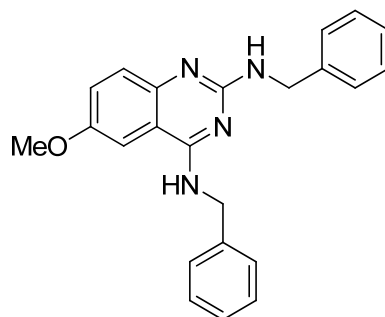




KSC-16-166

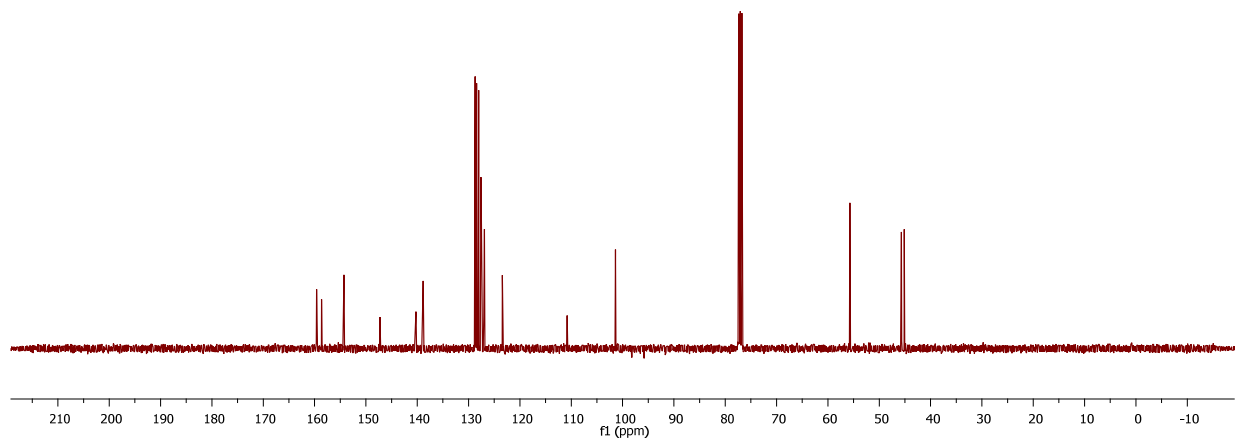
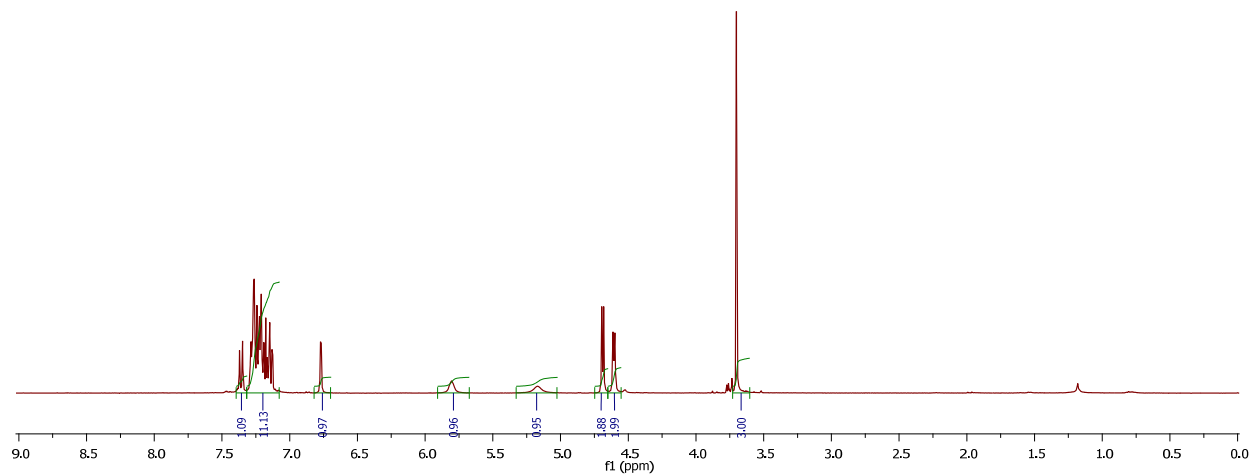
***N*²,*N*⁴-Dibenzyl-7-methoxyquinazoline-2,4-diamine (S137).** Yield: 47.0 mg, 58%. ¹H NMR (400 MHz, CDCl₃) δ 7.33 – 7.08 (m, 11H), 6.75 (s, 1H), 6.57 (dd, *J* = 2.5, 8.9 Hz, 1H), 5.72 (s, br. 1H), 5.32 (s, br. 1H), 4.64 (d, *J* = 5.5 Hz, 2H), 4.61 (d, *J* = 5.8 Hz, 2H), 3.72 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 163.4, 160.1, 159.9, 154.5, 140.1, 138.9, 128.7, 128.5, 128.0, 127.6, 127.5, 127.0, 122.3, 112.7, 105.2, 104.9, 55.4, 45.6, 45.0. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (*M*+*H*) 371.1872; found 371.1872.

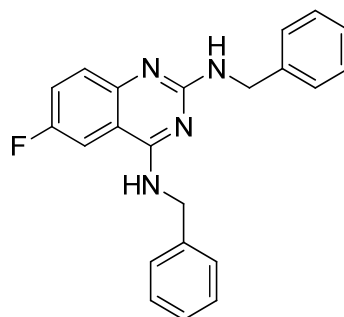




KSC-16-172

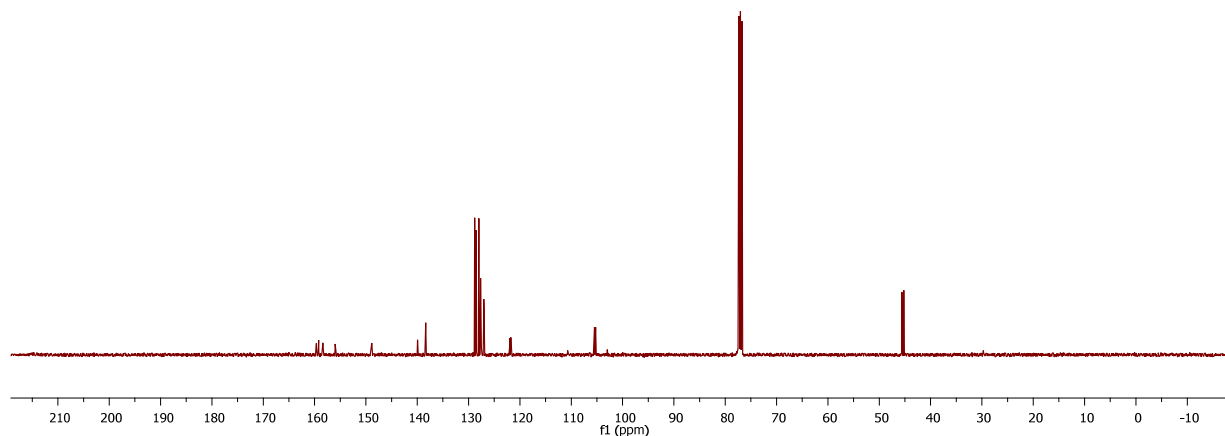
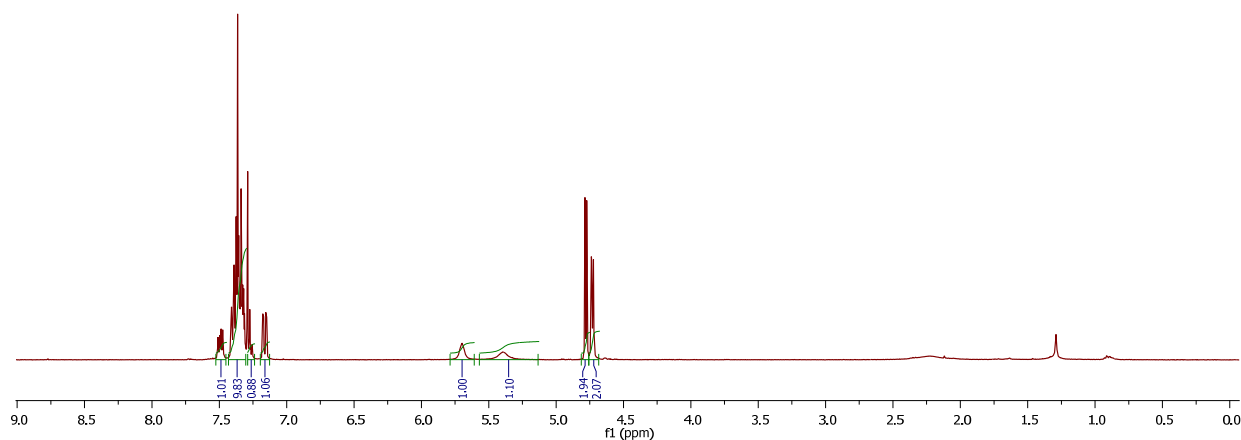
***N*²,*N*⁴-Dibenzyl-6-methoxyquinazoline-2,4-diamine (S138).** Yield: 22.5 mg, 46%. ¹H NMR (400 MHz, CDCl₃) δ 7.36 (d, *J* = 9.1 Hz, 1H), 7.32 – 7.08 (m, 11H), 6.77 (d, *J* = 2.7 Hz, 1H), 5.80 (s, 1H), 5.17 (s, 1H), 4.69 (d, *J* = 5.4 Hz, 2H), 4.61 (d, *J* = 5.4 Hz, 2H), 3.70 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 159.6, 158.6, 154.3, 147.3, 140.2, 138.9, 128.7, 128.4, 128.0, 127.6, 127.5, 127.0, 126.9, 123.4, 110.8, 101.4, 55.7, 45.7, 45.1. HRMS (*m/z*): calcd for C₂₃H₂₃N₄O (*M*+*H*) 371.1872; found 371.1874.

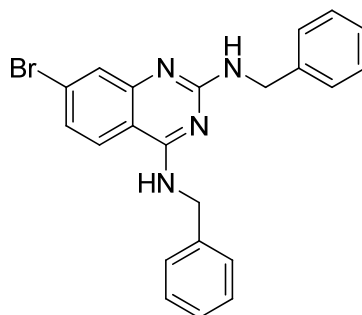




KSC-16-175

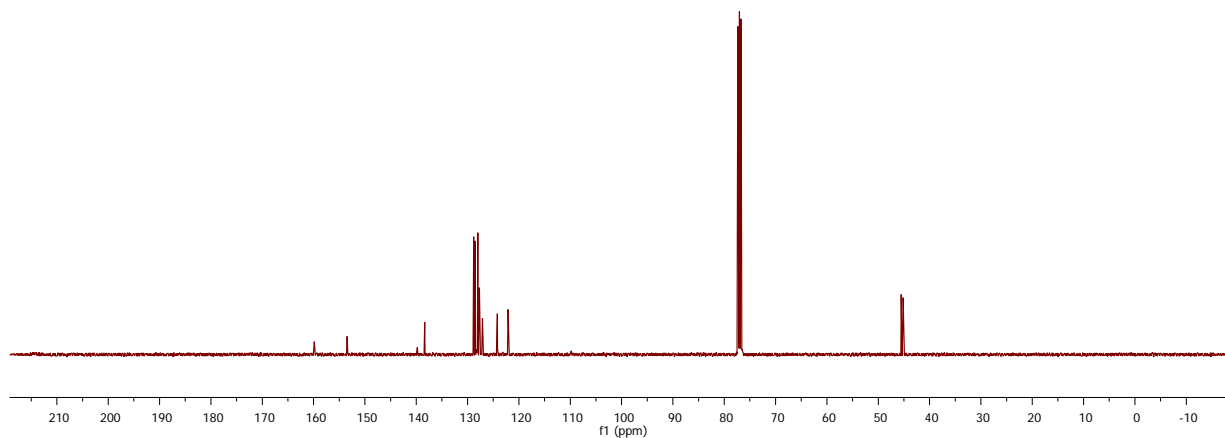
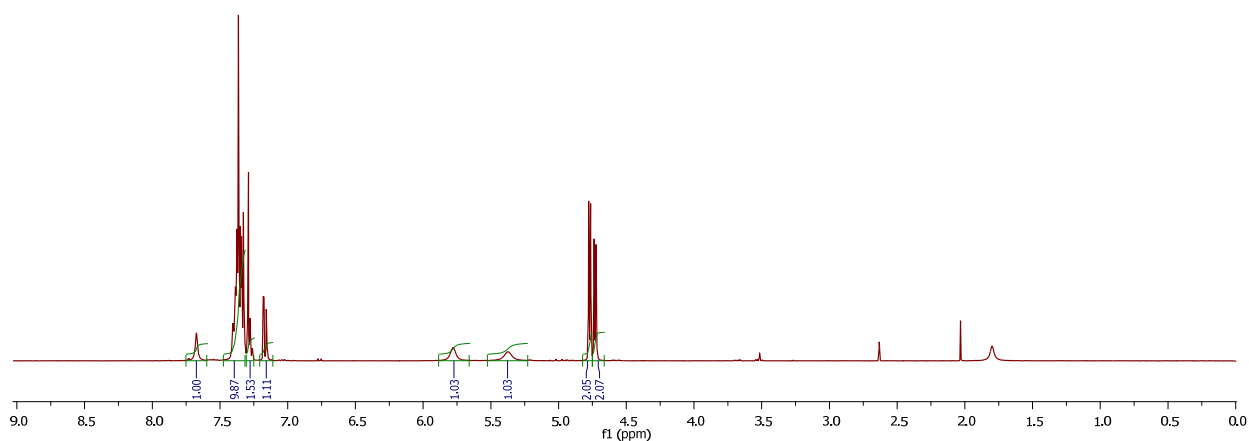
***N*²,*N*⁴-Dibenzyl-6-fluoroquinazoline-2,4-diamine (S139).** Yield: 12 mg, 24%. ¹H NMR (400 MHz, CDCl₃) δ 7.49 (dd, *J* = 5.2, 9.1 Hz, 1H), 7.43 – 7.30 (m, 10H), 7.27 (d, *J* = 7.2 Hz, 1H), 7.16 (dd, *J* = 2.7, 9.0 Hz, 1H), 5.70 (s, br. 1H), 5.40 (s, br. 1H), 4.78 (d, *J* = 5.4 Hz, 2H), 4.73 (d, *J* = 5.7 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 159.7, 159.6, 159.2, 158.4, 156.0, 148.9, 140.0, 138.4, 128.8, 128.5, 128.0, 127.7, 127.6, 127.0, 122.0, 121.8, 110.7, 110.6, 105.5, 105.3, 103.0, 45.6, 45.2. HRMS (*m/z*): calcd for C₂₂H₂₀FN₄ (*M*+*H*) 359.1672; found 359.1672.

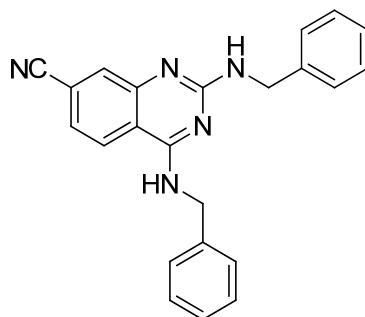




KSC-16-122

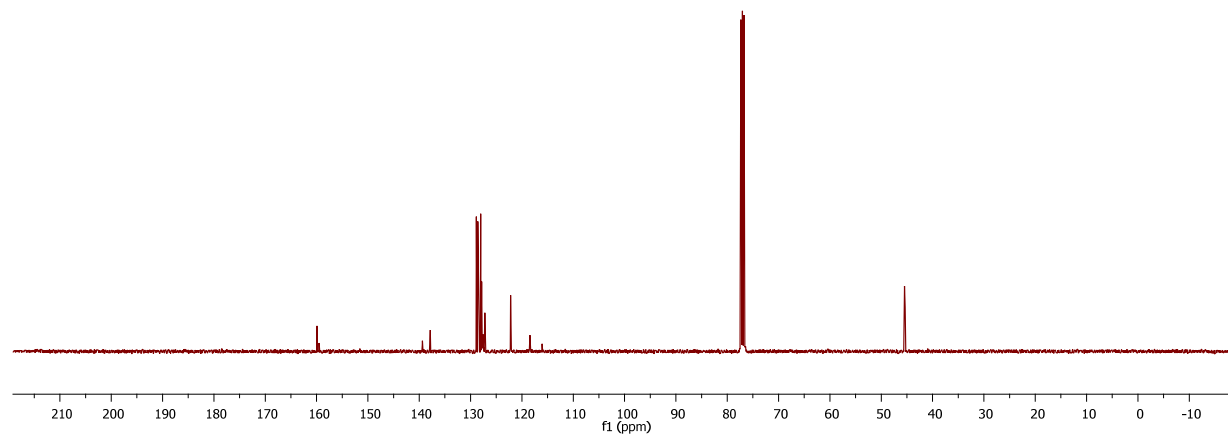
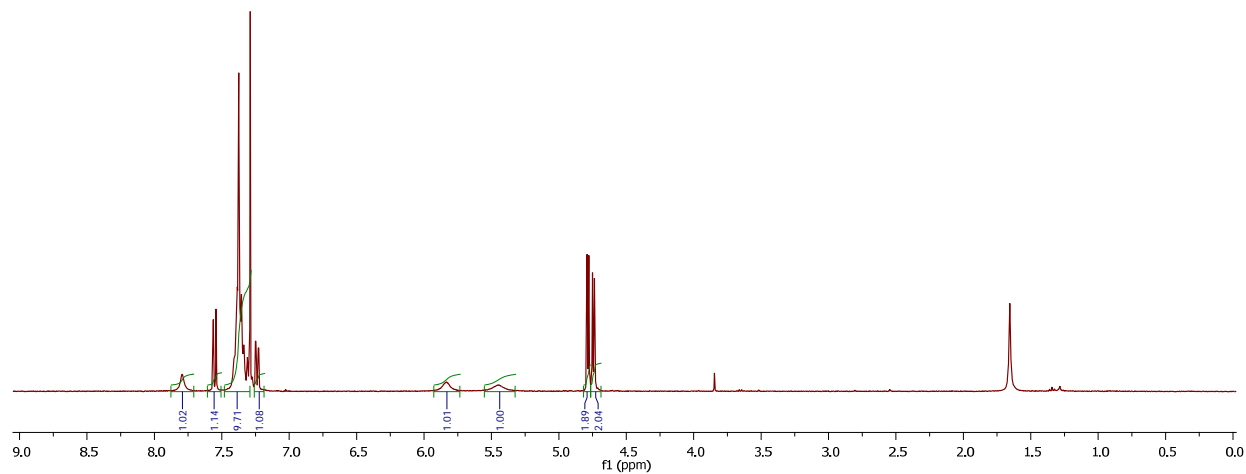
***N*²,*N*⁴-Dibenzyl-7-bromoquinazoline-2,4-diamine (S140).** Yield: 12.7 mg, 17%. ¹H NMR (400 MHz, CDCl₃) δ 7.67 (s, br. 1H), 7.47 – 7.32 (m, 10H), 7.31 – 7.25 (m, 1H), 7.17 (dd, *J* = 1.9, 8.6, 1H), 5.78 (s, br. 1H), 5.37 (s, br. 1H), 4.77 (d, *J* = 5.4 Hz, 2H), 4.73 (d, *J* = 5.9 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 159.9, 159.9, 153.5, 139.8, 138.3, 128.8, 128.5, 128.0, 127.7, 127.6, 127.2, 127.1, 124.2, 122.1, 45.5, 45.2. HRMS (*m/z*): calcd for C₂₂H₂₀BrN₄ (*M*+*H*) 419.0871 and 421.0851; found 421.0845.



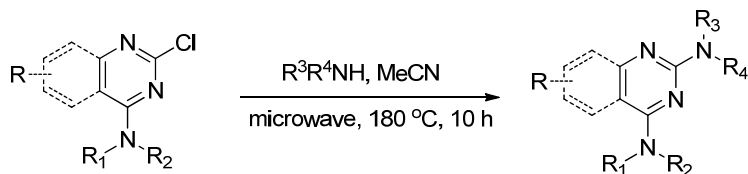


KSC-16-167c

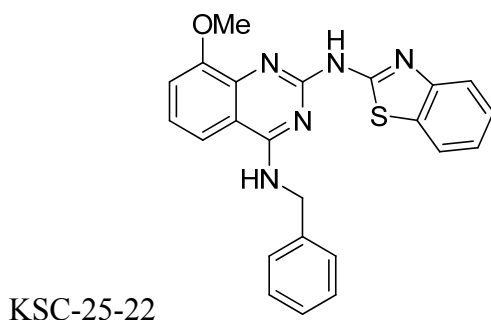
2,4-Bis(benzylamino)quinazoline-7-carbonitrile (S141). Yield: 12.3 mg, 15%. ^1H NMR (400 MHz, CDCl_3) δ 7.79 (s, br. 1H), 7.55 (d, $J = 8.3$ Hz, 1H), 7.47 – 7.30 (m, 10H), 7.24 (dd, $J = 1.6$, 8.3 Hz, 1H), 5.83 (s, 1H), 5.55 – 5.32 (m, 1H), 4.78 (d, $J = 5.4$ Hz, 2H), 4.74 (d, $J = 6.0$ Hz, 2H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.9, 159.5, 139.4, 137.9, 128.9, 128.6, 128.0, 127.9, 127.6, 127.2, 122.2, 118.4, 116.1, 45.5, 45.4. HRMS (m/z): calcd for $\text{C}_{23}\text{H}_{20}\text{N}_5$ ($\text{M}+\text{H}$) 366.1719; found 366.1719.



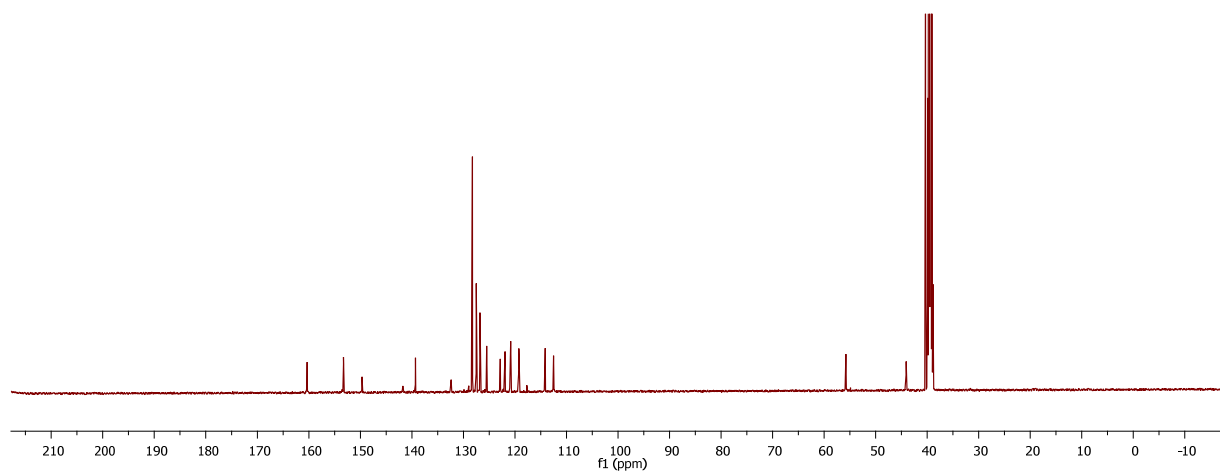
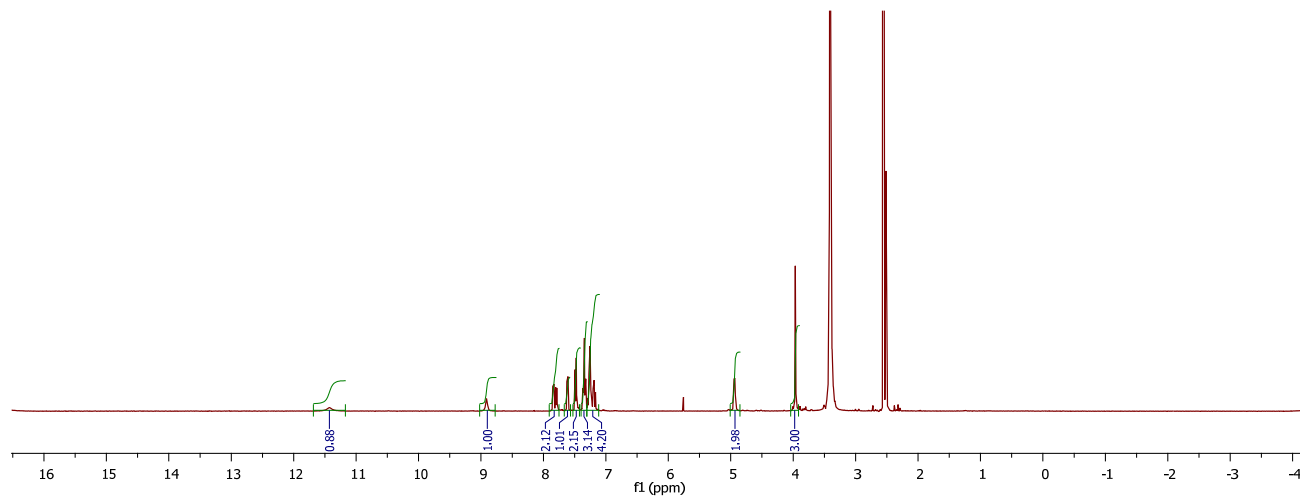
General procedure D: representative protocol for the synthesis of quinazoline analogues of less nucleophilic amines, synthesis and characterization for S166, S161, S163 (**31**), S164, S167 (**19**), S168.

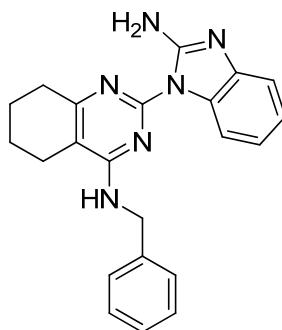


Scheme S4: Synthesis of quinazoline analogues of less nucleophilic amines



***N*²-(Benzo[*d*]thiazol-2-yl)-*N*⁴-benzyl-8-methoxyquinazoline-2,4-diamine (S166).** To a suspension of *N*-benzyl-2-chloro-8-methoxyquinazolin-4-amine (15.0 mg, 50 μmol) in CH₃CN (1 mL) was added 2-aminobenzo[*d*]thiazole (15.0 mg, 0.1 mmol, 2 equiv.). The mixture was heated to 180 °C for 10 h under microwave irradiation. The solvent was removed under vacuum, the residue was suspended in EtOAc, washed with saturated NaHCO₃, and the layers were separated. The organic layer was dried over MgSO₄ and concentrated under vacuum. The residue was purified by reverse phase preparative HPLC to give the product (7.2 mg, 35%). ¹H NMR (400 MHz, DMSO) δ 11.43 (s, br, 1H), 8.91 (s, 1H), 7.91 – 7.75 (m, 2H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.48 (d, *J* = 7.2 Hz, 2H), 7.40 – 7.30 (m, 3H), 7.30 – 7.11 (m, 4H), 4.94 (d, *J* = 5.6 Hz, 2H), 3.96 (s, 3H). ¹³C NMR (126 MHz, DMSO) δ 160.3, 160.2, 153.5, 153.3, 149.7, 141.8, 139.3, 132.4, 128.3, 127.5, 126.8, 125.5, 122.9, 121.9, 120.8, 119.2, 117.7, 114.1, 112.5, 55.8, 44.1. HRMS (*m/z*): calcd for C₂₃H₂₀N₅OS (M+H) 414.1389; found 414.1390.

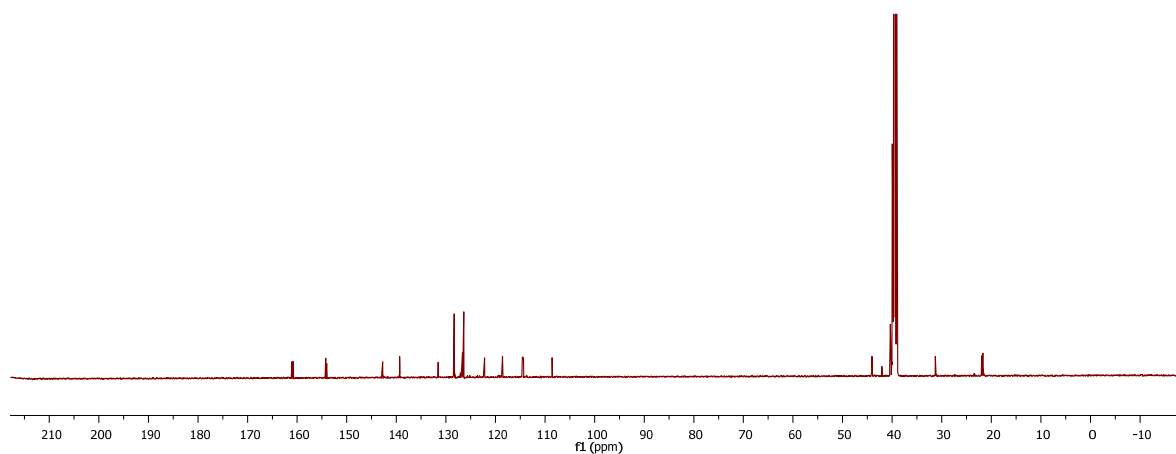
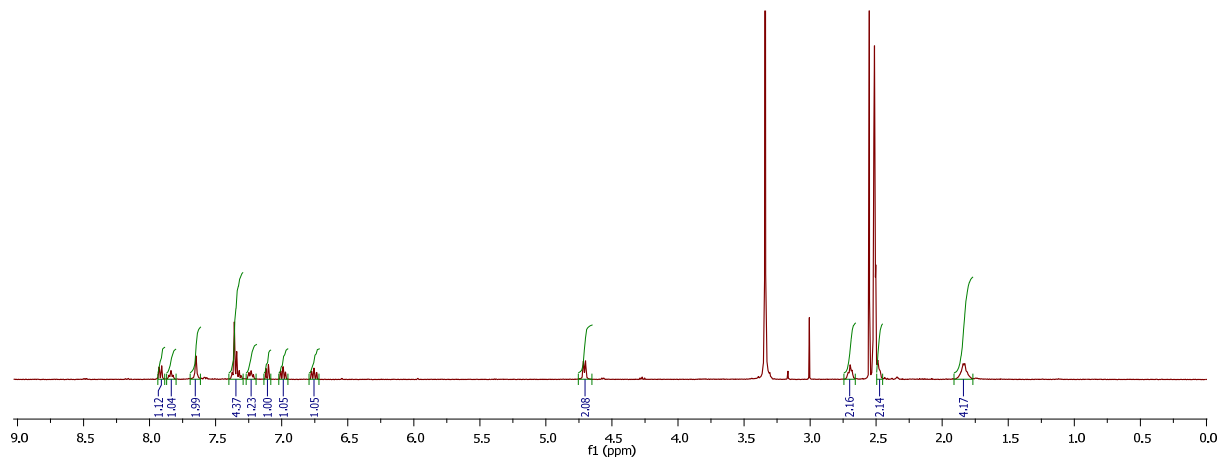


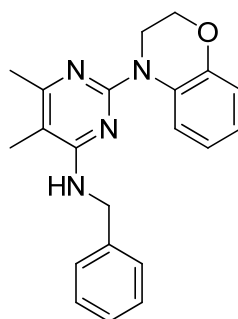


KSC-25-31

2-(2-Amino-1H-benzo[d]imidazol-1-yl)-N-benzyl-5,6,7,8-tetrahydroquinazolin-4-amine

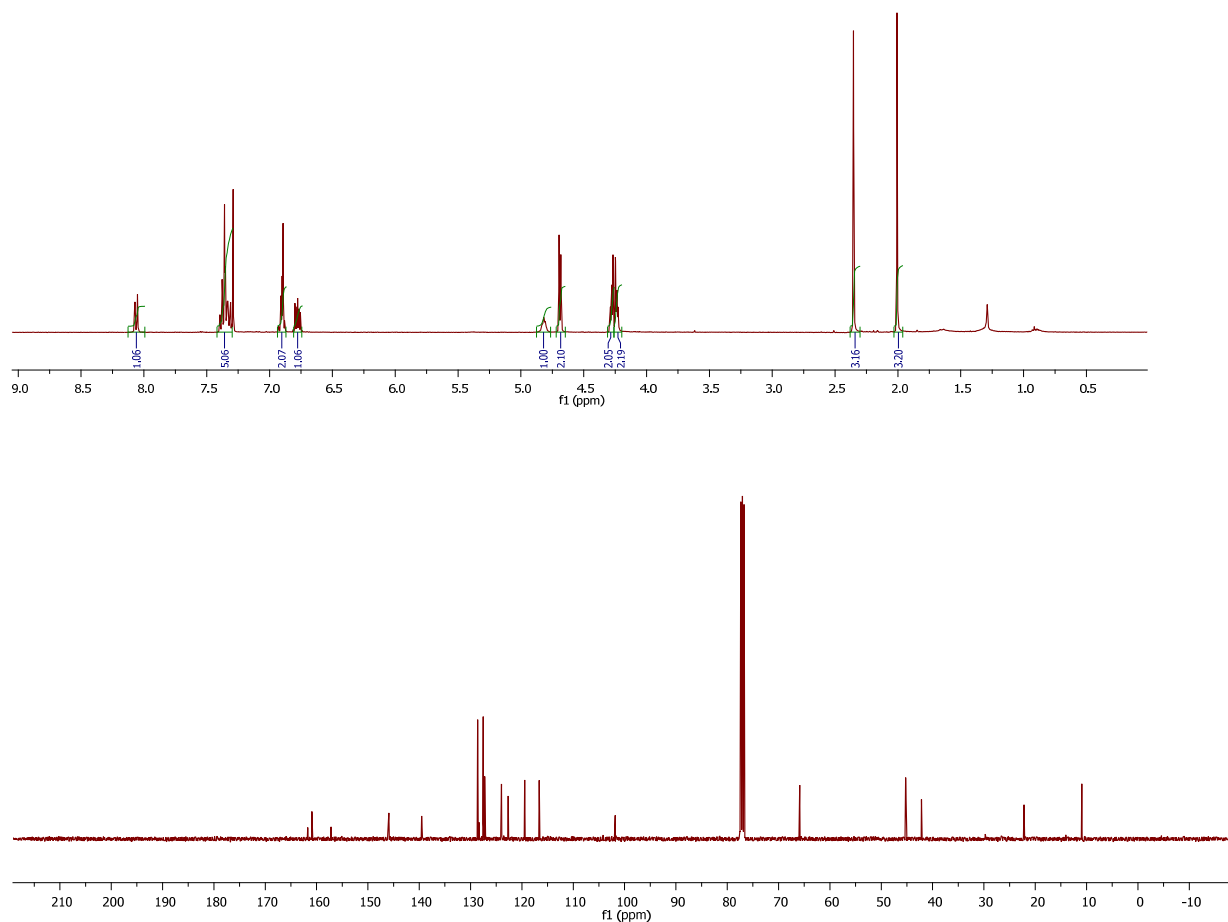
(S161, 18). Yield: 1.8 mg, 12%. ^1H NMR (400 MHz, DMSO) δ 7.92 (d, $J = 7.4$ Hz, 1H), 7.84 (s, 1H), 7.65 (s, 2H), 7.40 – 7.29 (m, 4H), 7.23 (s, 1H), 7.11 (d, $J = 7.1$ Hz, 1H), 6.99 (t, $J = 7.0$ Hz, 1H), 6.79 – 6.72 (m, 1H), 4.71 (d, $J = 6.0$ Hz, 2H), 2.70 (s, br. 2H), 2.49 (s, br. 2H), 1.83 (s, br. 4H). ^{13}C NMR (126 MHz, DMSO) δ 161.0, 160.8, 154.3, 154.1, 142.8, 139.3, 131.6, 128.3, 126.7, 126.4, 122.2, 118.6, 114.6, 114.3, 108.6, 44.1, 31.3, 21.9, 21.7, 21.6. HRMS (m/z): calcd for $\text{C}_{22}\text{H}_{23}\text{N}_6$ ($\text{M}+\text{H}$) 371.1984; found 371.1989.

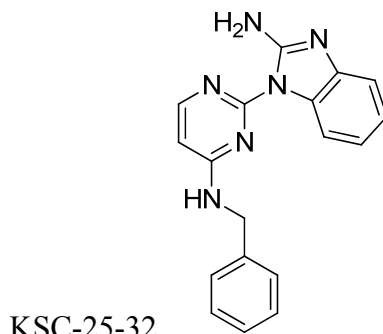




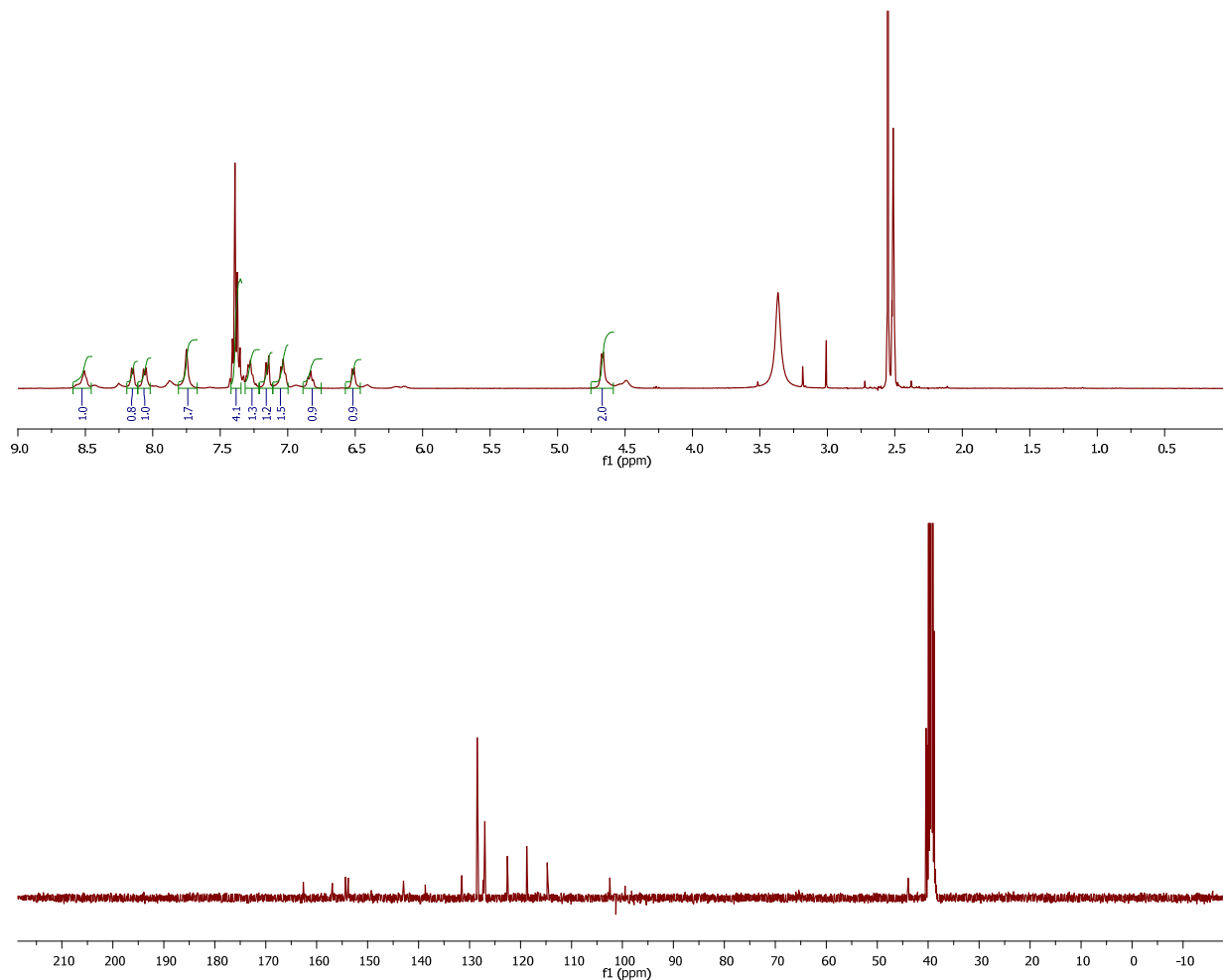
KSC-25-24

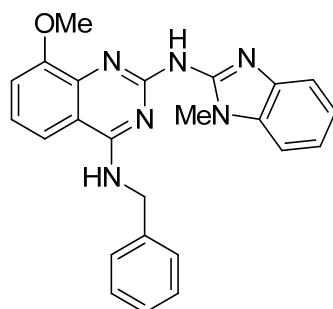
2-(2H-Benzo[b][1,4]oxazin-4(3H)-yl)-N-benzyl-5,6-dimethylpyrimidin-4-amine (S163 or 31).
 (Reaction time = 6 h) Yield: 6.5 mg, 46%. ^1H NMR (400 MHz, CDCl_3) δ 8.13 – 7.99 (m, 1H), 7.42 – 7.30 (m, 5H), 6.94 – 6.87 (m, 2H), 6.81 – 6.74 (m, 1H), 4.82 (s, 1H), 4.69 (d, J = 5.6 Hz, 2H), 4.31 – 4.26 (m, 2H), 4.29 – 4.23 (m, 2H), 2.35 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 161.7, 160.9, 157.2, 145.9, 139.5, 128.6, 128.4, 127.5, 127.2, 124.0, 122.7, 119.5, 116.6, 101.8, 65.9, 45.3, 42.2, 22.2, 10.9. HRMS (m/z): calcd for $\text{C}_{21}\text{H}_{23}\text{N}_4\text{O}$ ($\text{M}+\text{H}$) 347.1872; found 347.1872.





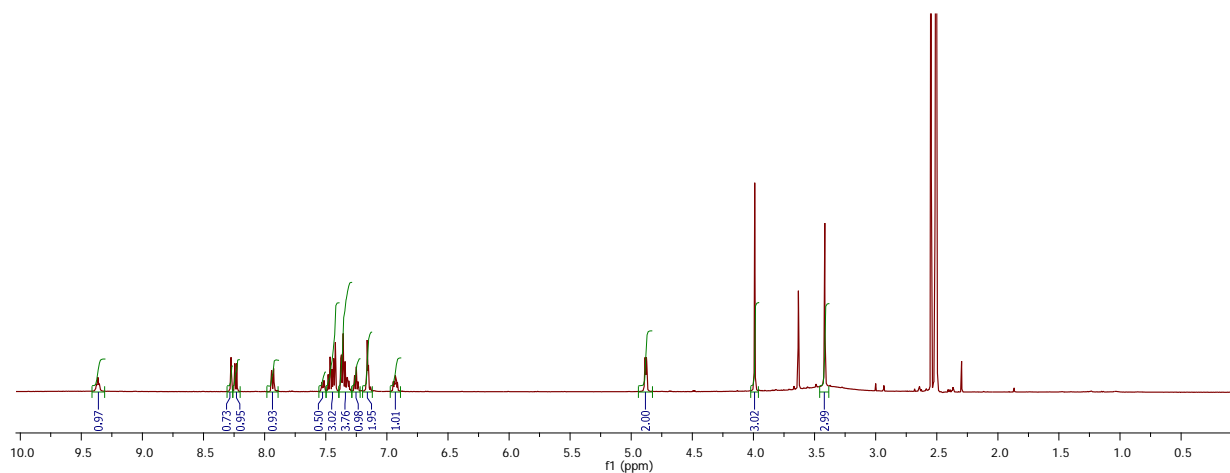
1-(4-(Benzylamino)pyrimidin-2-yl)-1H-benzo[d]imidazol-2-amine (S164). Yield: 11.7 mg, 48%. ^1H NMR (400 MHz, DMSO) δ 8.51 (s, 1H), 8.16 (s, 1H), 8.05 (s, 1H), 7.75 (s, 2H), 7.41 – 7.35 (m, 4H), 7.28 (s, 1H), 7.15 (d, $J = 7.6$ Hz, 1H), 7.05 – 7.02 (m, 1H), 6.83 (t, $J = 7.8$ Hz, 1H), 6.51 (d, $J = 5.8$ Hz, 2H), 4.66 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 162.6, 156.9, 154.4, 153.8, 143.0, 138.7, 131.5, 128.5, 127.0, 122.6, 118.8, 114.7, 114.6, 102.5, 101.3, 43.9. HRMS (m/z): calcd for $\text{C}_{18}\text{H}_{17}\text{N}_6$ ($\text{M}+\text{H}$) 317.1515; found 317.1520.

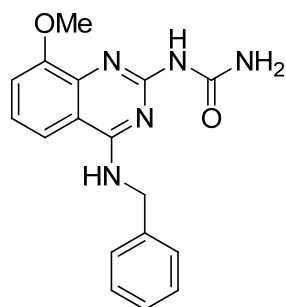




KSC-25-21

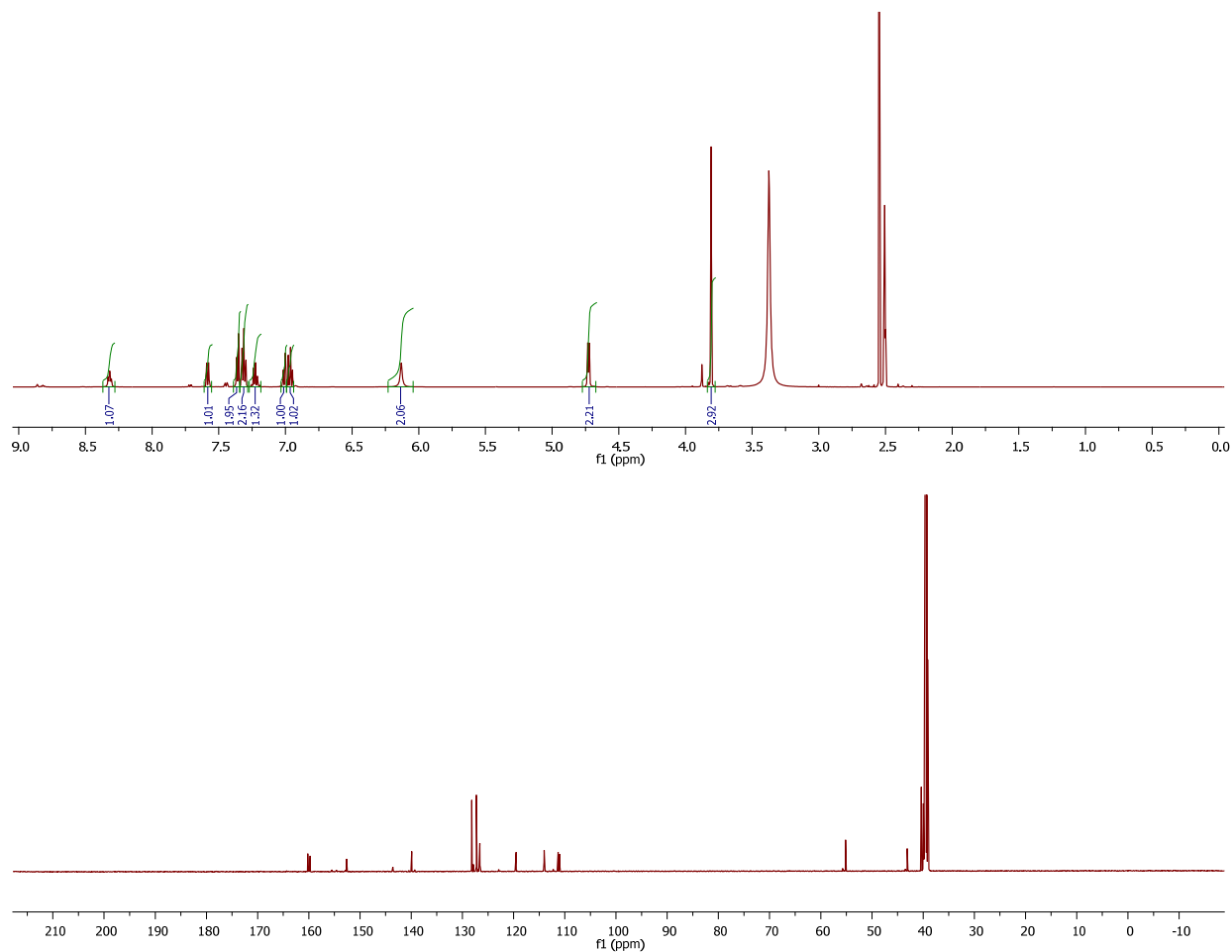
***N*⁴-Benzyl-8-methoxy-*N*²-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)quinazoline-2,4-diamine (S167 or 19).** Yield: 3.9 mg, 19%. ¹H NMR (500 MHz, DMSO) δ 9.36 (s, 1H), 8.28 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 7.9 Hz, 1H), 7.51 (s, 1H), 7.50 – 7.39 (m, 2H), 7.35 (td, *J* = 2.7, 9.5 Hz, 3H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.16 (d, *J* = 5.4 Hz, 2H), 6.93 (s, 1H), 4.88 (d, *J* = 5.7 Hz, 2H), 3.99 (s, 3H), 3.42 (s, 3H). HRMS (*m/z*): calcd for C₂₄H₂₃N₆O (*M*+*H*) 411.1933; found 411.1937.



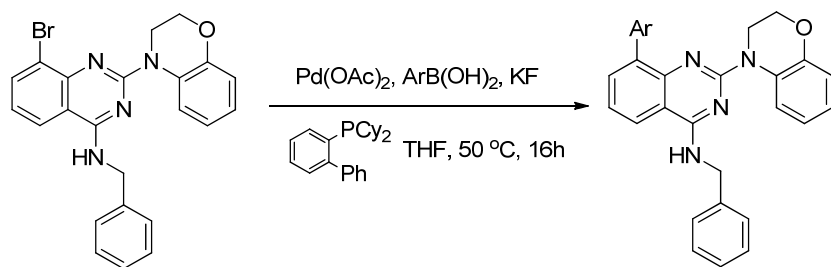


KSC-25-12

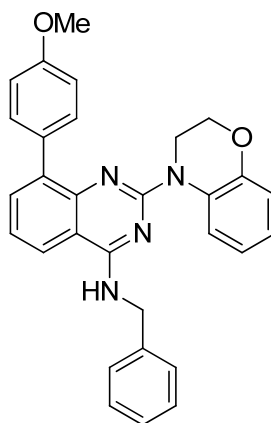
1-(4-(Benzylamino)-8-methoxyquinazolin-2-yl)urea (S168). (Reaction time = 3 h) Yield: 4.7 mg, 47%. ^1H NMR (500 MHz, DMSO) δ 8.32 (d, J = 7.1 Hz, 1H), 7.58 (dd, J = 1.3, 8.2 Hz, 1H), 7.36 (d, J = 7.0 Hz, 2H), 7.31 (dd, J = 4.9, 10.3 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.01 (d, J = 6.7 Hz, 1H), 6.96 (t, J = 7.9 Hz, 1H), 6.13 (s, 2H), 4.73 (d, J = 5.9 Hz, 2H), 3.81 (s, 3H). ^{13}C NMR (126 MHz, DMSO) δ 160.2, 159.8, 152.6, 143.6, 139.9, 128.2, 127.9, 127.3, 126.6, 119.5, 114.0, 111.3, 111.0, 55.2, 43.1. HRMS (m/z): calcd for $\text{C}_{17}\text{H}_{18}\text{N}_5\text{O}_2$ ($M+H$) 324.1460; found 324.1449.



General procedure E: representative protocol for the synthesis of quinazoline analogues via a Suzuki coupling route, synthesis and characterization for S153 (**36**) and S149.

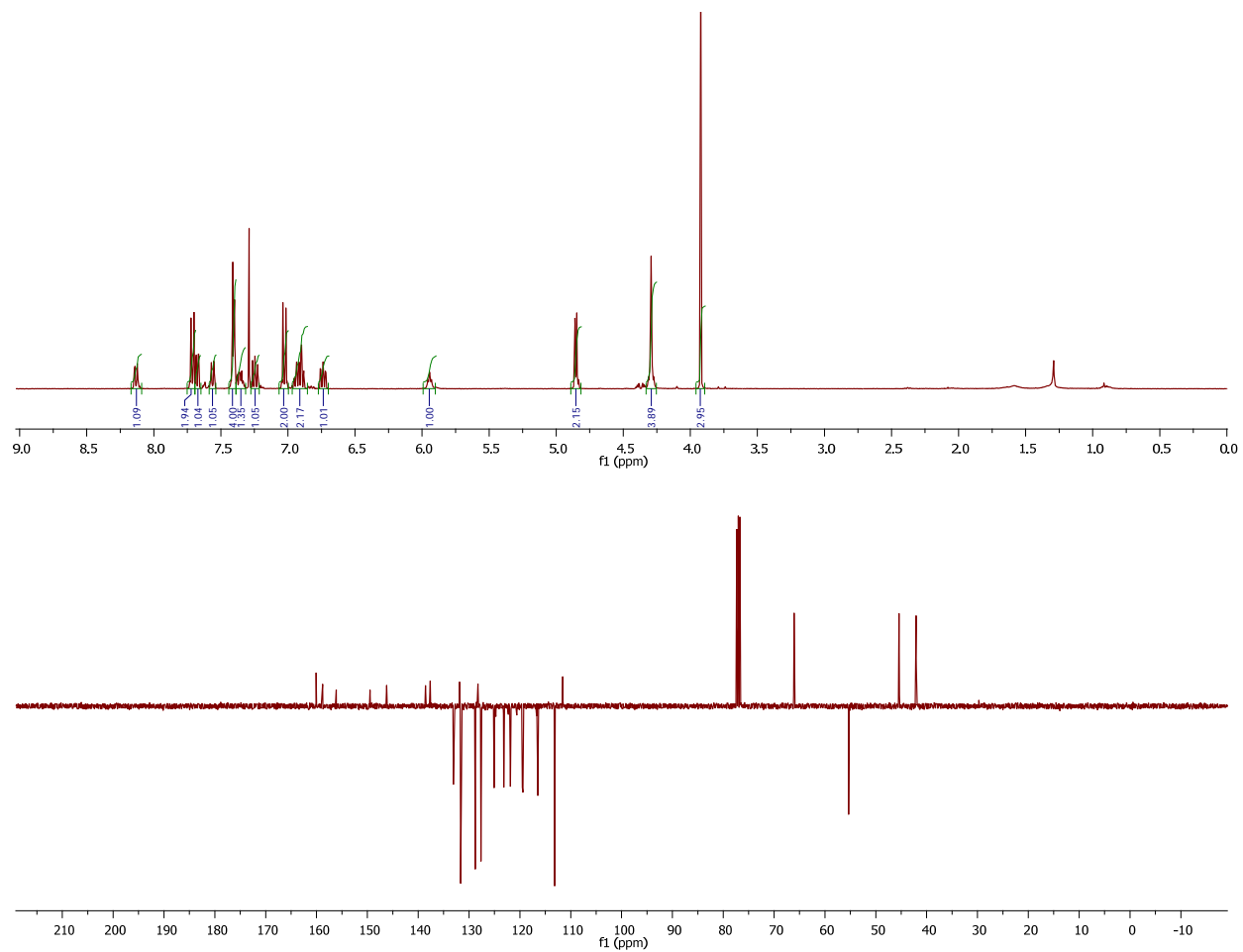


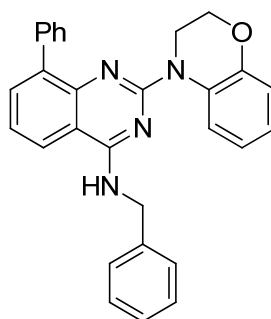
Scheme S5. Derivatization of quinazoline analogues via a Suzuki coupling route.



KSC-16-268

2-(2H- Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-(4-methoxyphenyl)quinazolin-4-amine (S153 or 36). A mixture of 2-(2H-benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-bromoquinazolin-4-amine (12.0 mg, 26.8 μ mol), palladium acetate (0.6 mg, 2.7 μ mol), [1,1'-biphenyl]-2-ylidicyclohexylphosphine (1.9 mg, 5.4 μ mol), 4-methoxyphenylboronic acid (6.1 mg, 40.2 μ mol), potassium fluoride (4.7 mg, 80.5 μ mol) in 0.5 mL of THF was heated at 50 °C for 16 h. The mixture was diluted with EtOAc and washed with water. The organic phase was concentrated and purified by SGC (DCM/MeOH = 1:9, R_f = 0.5). Yield: 12 mg, 94%. ¹H NMR (400 MHz, CDCl₃) δ 8.17 – 8.09 (m, 1H), 7.75 – 7.69 (m, 2H), 7.68 (dd, *J* = 1.4, 7.3 Hz, 1H), 7.56 (dd, *J* = 1.3, 8.2 Hz, 1H), 7.40 (dd, *J* = 1.9, 3.5 Hz, 4H), 7.39 – 7.32 (m, 1H), 7.28 – 7.21 (m, 1H), 7.07 – 7.00 (m, 2H), 6.92 (dtd, *J* = 1.6, 8.1, 9.9 Hz, 2H), 6.77 – 6.70 (m, 1H), 5.94 (s, 1H), 4.85 (t, *J* = 5.3 Hz, 2H), 4.33 – 4.25 (m, 4H), 3.92 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.1, 158.8, 156.1, 149.5, 146.2, 138.6, 137.6, 133.1, 131.9, 131.6, 128.8, 128.2, 127.7, 127.6, 125.1, 123.2, 121.9, 119.5, 119.4, 116.5, 113.2, 111.6, 66.1, 55.4, 45.5, 42.1. HRMS (*m/z*): calcd for C₃₀H₂₇N₄O₂ (M+H) 475.2134; found 475.2135.





KSC-16-255

2-(2H-Benzo[*b*][1,4]oxazin-4(3H)-yl)-N-benzyl-8-phenylquinazolin-4-amine (S149). Yield: 3.9 mg, 33%. ^1H NMR (400 MHz, CDCl_3) δ 8.03 (d, $J = 7.0$ Hz, 1H), 7.69 – 7.55 (m, 3H), 7.50 (d, $J = 7.0$ Hz, 1H), 7.38 (t, $J = 7.4$ Hz, 2H), 7.34 – 7.22 (m, 5H), 7.18 – 7.11 (m, 1H), 6.79 (dt, $J = 6.6, 8.1$ Hz, 2H), 6.62 (dd, $J = 4.3, 10.9$ Hz, 1H), 5.86 (s, 1H), 4.76 (d, $J = 5.4$ Hz, 2H), 4.18 (s, 4H). ^{13}C NMR (126 MHz, CDCl_3) δ 160.0, 156.1, 149.5, 146.2, 139.5, 138.5, 138.1, 133.5, 130.5, 128.8, 128.2, 127.7, 127.7, 127.6, 126.9, 125.0, 123.2, 121.8, 120.0, 119.4, 116.4, 111.6, 66.0, 45.5, 42.0. HRMS (m/z): calcd for $\text{C}_{29}\text{H}_{25}\text{N}_4\text{O}$ ($\text{M}+\text{H}$) 445.2028; found 445.2025.

